12 Meningococcal disease

Key information

Mode of transmission	By respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.
Incubation period	2–10 days, commonly 3–4 days.
Period of communicability	Therapy with cefotaxime, ceftriaxone, rifampicin, or ciprofloxacin eradicates *N. meningitidis* from mucosal surfaces within 24 hours, and the case is no longer considered infectious.
Available vaccines	Meningococcal group C conjugate (MenCCV): • NeisVac-C. Quadrivalent meningococcal conjugate (MCV4): • Menactra (MCV4-D) – conjugated to diphtheria toxoid • Nimenrix (MCV4-T) – conjugated to tetanus toxoid.
Dose, presentation, route	0.5 mL per dose. Presentation: • MenCCV: pre-filled syringe • MCV4-D: vial • MCV4-T: vaccine vial and pre-filled syringe. MCV4-T must be reconstituted before use. Intramuscular injection.
Funded vaccine indications	MCV4-D (Menactra) or MenCCV (NeisVac-C) for: • patients pre- or post-splenectomy or with functional asplenia • patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited) or pre- or post-solid organ transplant • HSCT (bone marrow transplant) patients • patients following immunosuppression • close contacts of meningococcal cases (of relevant serotype).
Vaccine efficacy/ effectiveness	MenCCV: 83–100% effectiveness. Marked reduction in disease incidence when used in population-wide programmes. Immunity wanes with time. MCV4: 80–85% effectiveness; 2–5 years after vaccination, effectiveness wanes to 50–60%.

Continued overleaf

Public health measures	Cases: must be notified upon suspicion. Administer antibiotics as soon as possible, often prior to transfer to hospital. Contacts: administer antibiotic prophylaxis preferably within 24 hours of the initial diagnosis, but recommended up to 14 days after the diagnosis of illness.

12.1 Bacteriology

Meningococcal disease is caused by *Neisseria meningitidis*, a gram-negative bacterium, and is an important cause of sepsis and meningitis. Worldwide, the most important serogroups of meningococci are groups A, B, C, W135 and Y. Groups B and C are the most important types seen in children and young adults in New Zealand. Group A is an important epidemic strain, particularly in Africa and the Middle East. Serotype distribution patterns differ between countries. W135 and Y group organisms are seen as rare causes of bacteraemia and pneumonia in the elderly.

Spread from person to person is by respiratory droplets or direct contact with nasopharyngeal secretions, from a carrier or case.

12.2 Clinical features

Table 12.1 below describes the symptoms and signs of meningococcal disease – individuals may present with some or all of these. Meningococcal bacteraemia is more common than meningitis, and the illness may be a mild non-specific illness or a rapidly progressive illness with fatal outcome.

Table 12.1: Symptoms and signs of meningococcal disease

Adolescents and adults	Young infants and children
Sepsis syndrome Nausea Vomiting Meningism Rash – petechial or purpuric or maculopapular; a rash may not be present in the early stages of the disease and is absent in about one-third of cases Sleepy, difficult to rouse Arthralgia and myalgia Occasionally in young adults, irrational behaviour	As for adolescents and adults, plus the following: • bulging fontanelle • tachycardia • altered responsiveness • irritability and/or floppiness • refusing drinks or feeds • poor peripheral perfusion
Notify all suspected cases as soon as possible to the local medical officer of health. This includes out-of-hours notification.	

Meningococcal disease covers a spectrum, from chronic septic arthritis and minor rash to fulminant sepsis and meningitis. Classic meningococcal sepsis frequently presents with sudden onset of fever and rash. Septic shock may rapidly ensue. Meningitis can occur with and without signs of sepsis. In fulminant cases, disseminated intravascular coagulation, shock, coma and death can occur within a few hours despite appropriate treatment.

Because of the fulminant nature of meningococcal sepsis, antibiotics (Table 12.2) should be administered as soon as possible, often prior to transfer to hospital. Antibiotics given prior to transfer should be clearly noted on the clinical information that accompanies the patient to hospital.

Table 12.2: Recommended antibiotics for suspected cases

Antibiotic	Dosage
Benzylpenicillin*	Adults: 1.2 g (2 MU) IV (or IM) Children: 50 mg/kg IV (or IM)
Amoxycillin	Adults: 1–2 g IV (or IM) Children 50 mg/kg IV (or IM)

* Patients with a documented history of anaphylaxis to penicillin and who are suspected of suffering from meningococcal disease should be sent immediately to hospital without pre-admission antibiotics.

12.3 Epidemiology

12.3.1 Global burden of disease

Incidence and serotypes

Introduction of a serogroup A conjugate vaccine has had a dramatic impact on disease in sub-Saharan Africa. Before the introduction the vaccine, Group A disease caused massive epidemics in sub-Saharan Africa (the 'meningitis belt'), with incidence ranging from 10 to 25 per 100,000 during non-epidemic periods and up to 1,000 per 100,000 during epidemic years.[1]

The incidence in Canada, the US and Europe varies substantially by country, ranging from 0.18 per 100,000 to 3 per 100,000 persons per year.[1] The serotype distribution varies by age, location and time, with types B, C and Y accounting for most of the reported cases.[2] Group B disease is often the most common serotype causing infection, and can cause epidemics that start slowly and persist for five or more years. Group C meningococci have been associated with small clusters of meningococcal disease cases in schools and universities.

Risk groups

Those particularly at risk of meningococcal disease are children aged under 5 years, although all age groups can be infected. There is a higher case fatality rate in adults. Most infection occurs in healthy people, but those with a deficiency of terminal components of complement (C5–9), properdin deficiency or asplenia are at particular risk of recurrent meningococcal disease. Individuals with infection caused by an uncommon serogroup or recurrent disease should be investigated.

Close contacts of primary cases of meningococcal infection are at increased risk of developing infection, such as within families,[3] early childhood education services, semi-closed communities, schools, correctional facilities and military recruit camps. Students living in hostel accommodation may also be at higher risk.[4, 5, 6] In health care settings, only those with close exposure to oropharyngeal secretions of patients with meningococcal disease (as may occur during intubation or

resuscitation) and microbiology laboratory workers are considered to be at increased risk.

It is not possible to calculate the incubation period for meningococcal disease for sporadic cases. Secondary cases (ie, in contacts of known cases of meningococcal disease) usually occur within four days, but it can be up to 10 days. The infectivity of patients with meningococcal disease is markedly reduced after 24 hours of antibiotic therapy, although treatment with cefotaxime, ceftriaxone, rifampicin or ciprofloxacin is necessary to reliably eradicate nasopharyngeal carriage and hence relax infection prevention and control precautions (see section 12.8.2).

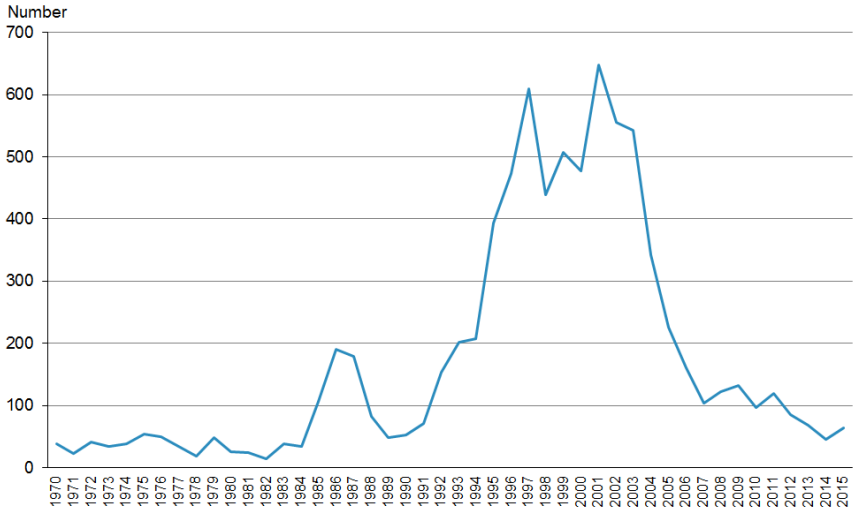
In high-income countries, nasopharyngeal carriage of *N. meningitidis* occurs in approximately 10 percent of the overall population, rising from 2 percent in children aged under 4 years to a peak of 24.5 percent to 32 percent among 15–24-year-olds, then declining with increasing age.[1] The relationship between risk factors for disease and those associated with carriage is incompletely understood.[1] Carriage prevalence does not predict the disease incidence nor the occurrence or severity of outbreaks, as most of the carried strains are non-encapsulated and do not cause disease.[1] Smoking, passive smoking, household crowding and upper respiratory tract infections increase carriage.

12.3.2 New Zealand epidemiology

Incidence and mortality

In 2015 the notification rate for meningococcal disease was 1.4 cases per 100,000 population, with a total of 64 cases notified (61 laboratory-confirmed).[7] This was slightly higher than the 2014 rate (1.0 per 100,000, 45 cases), but significantly lower than the peak rate experienced during the meningococcal disease epidemic (overall 16.7 per 100,000 but 200 per 100,000 in children under 12 months) in 2001. The annual number of notified cases of meningococcal disease in New Zealand since 1970 is shown in Figure 12.1. The epidemic from 1991 to 2007 was largely due to a single Group B subtype (B:4:P1.7b,4).

Figure 12.1: Notified cases of meningococcal disease, 1970–2015



Source: ESR

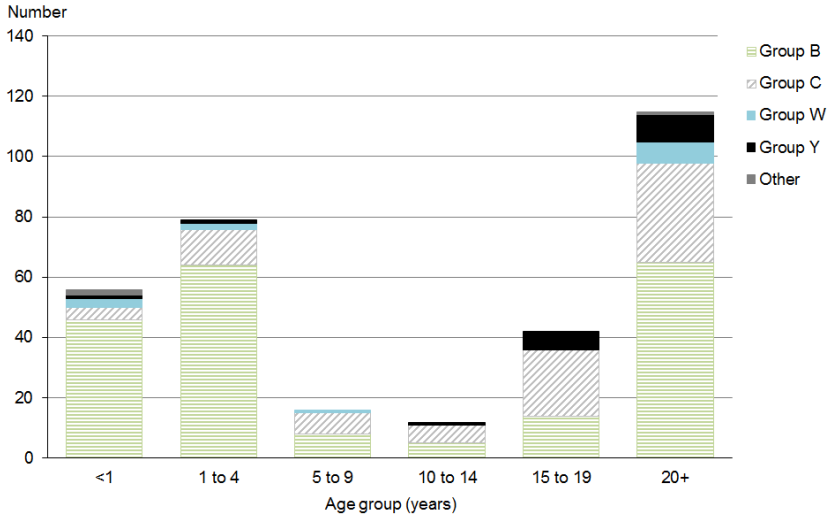
Meningococcal infection rates remain consistently higher in Māori and Pacific peoples compared with the total population. Māori had the highest disease rate in 2015 (2.9 per 100,000, 20 cases), followed by Pacific peoples (2.8 per 100,000, 8 cases).[7]

Household crowding is an important risk factor for meningococcal disease, independent of ethnicity.[8]

In 2015 the highest age-specific disease rates were among those aged under 1 year (22 per 100,000, 13 cases) and 1–4 years (6.9 per 100,000, 17 cases).[7]

Figure 12.2 shows the age distribution of the 320 strain-typed cases from 2011 to 2015. Group B strains were the most prevalent in all age groups except for the age group 15–19 years, in which Group C strains were the most prevalent.

Figure 12.2: Age distribution among strain-typed meningococcal disease cases, 2011–2015 cumulative data



Note: Other includes 2 cases with non-groupable strains (1 each in the <1 and 20+ age groups) and 1 case with a group 29E strain (in the <1 age group).

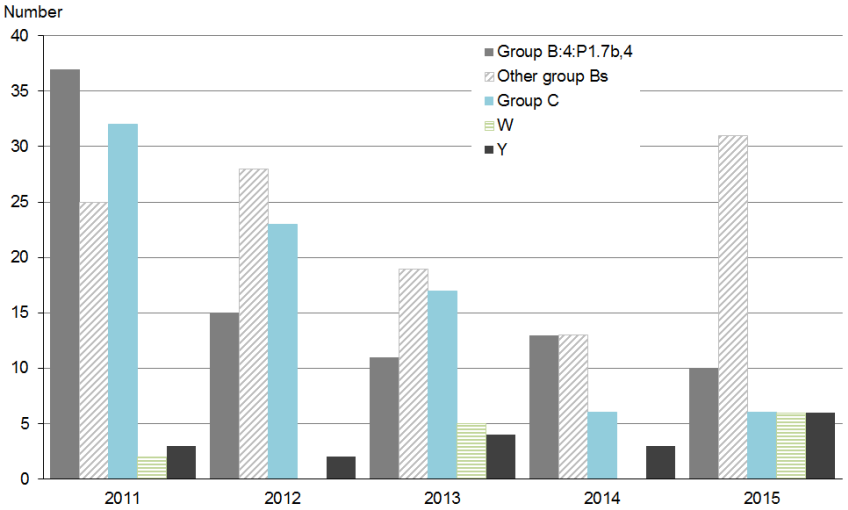
Source: ESR

Almost all cases (62/64) in 2015 were hospitalised. Four deaths were reported, giving a case fatality rate of 6.3 percent.[7]

Strain types

Strain type was determined for 59 of the 61 laboratory-confirmed cases.[7] Group B strains were the most prevalent in 2015, causing 69 percent of the confirmed cases (Figure 12.3). The group B strain (B:4:P1.7b,4) responsible for the epidemic caused 17 percent of all meningococcal disease in 2015 (10 of the 59 typed cases). The number of cases of meningococcal disease caused by group C strains has decreased since 2011 (Figure 12.3).

Figure 12.3: Groups and dominant subtypes among strain-typed meningococcal disease cases, 2011–2015



Note: Not shown in the figure are 2 cases with non-groupable strains (1 each in 2011 and 2013), and 1 case in 2014 with a group 29E strain.

Source: ESR

12.4 Vaccines

12.4.1 Introduction

Internationally, meningococcal vaccination programmes have been revolutionised by the development of conjugate vaccines, which allow vaccination in younger children and are associated with the development of herd immunity when used widely (see section 1.4.3 for more information about conjugate vaccines).

The monovalent (C) and quadrivalent (ACYW135) conjugate vaccines contain CRM_{197} or diphtheria or tetanus toxoid conjugate and are currently the only meningococcal vaccines available in New Zealand that can be effectively used in children aged under 2 years. Polysaccharide vaccines can offer three to five years' protection in adults, but they are generally regarded as inferior to conjugate vaccines. There are no polysaccharide vaccines registered (approved for use) and available (marketed) in New Zealand at the time of writing. Vaccination against

serogroups other than C (except serogroup B, which is not available in a conjugate vaccine) does not really offer much advantage in the New Zealand context, but those travelling to Africa, the Middle East and other areas with different serotype prevalence may benefit from broader protection. The meningococcal vaccines registered and available in New Zealand are summarised in Table 12.3 below.

Table 12.3: Meningococcal vaccines registered and available in New Zealand

Name (manufacturer)	Vaccine type
NeisVac-C (Pfizer NZ Ltd)	Meningococcal group C conjugate (MenCCV)
Menactra (Sanofi)	Quadrivalent meningococcal conjugate (MCV4-D) (contains serogroups A, C, Y, and W135)
Nimenrix (Pfizer NZ Ltd)	Quadrivalent meningococcal conjugate (MCV4-T) (contains serogroups A, C, Y, and W135)

Funded vaccines

No meningococcal vaccines are included on the routine Schedule but meningococcal group C conjugate and quadrivalent meningococcal conjugate vaccines are recommended and funded for certain individuals (see section 12.5).

Two meningococcal conjugate vaccines are funded for certain at-risk groups.

- Meningococcal group C conjugate vaccine MenCCV (NeisVac-C, Pfizer NZ Ltd) contains 10 µg of polysaccharide derived from the group C capsule, conjugated to 10–20 µg of tetanus toxoid. Other components include aluminium hydroxide and sodium chloride.
- Quadrivalent meningococcal conjugate vaccine MCV4-D (Menactra, Sanofi) contains 4 µg of each polysaccharide derived from the capsules of group A, C, Y and W135 *N. meningitidis* strains, each conjugated to diphtheria toxoid. Other components include sodium chloride and sodium phosphate.

Other vaccines

Quadrivalent meningococcal conjugate vaccines

A second quadrivalent meningococcal conjugate vaccine MCV4-T (Nimenrix, Pfizer NZ Ltd) is registered and available in New Zealand for individuals aged 12 months to 55 years.

MCV4-T contains 5 µg of each polysaccharide derived from the capsules of group A, C, Y and W135 *N. meningitidis* strains, conjugated to 44 µg of tetanus toxoid carrier protein. Other components and excipients include sodium chloride, trometamol and sucrose.

Group B meningococcal vaccines

Group B vaccines are not currently registered in New Zealand. A strain-specific group B meningococcal vaccine (MeNZB, Chiron/Novartis) containing outer membrane vesicles derived from the epidemic strain B:4:P1.7b,4 (NZ 98/254) was developed for epidemic control in New Zealand and used between 2004 and 2008. The vaccination programme ceased in 2008 because of a decline in the incidence of group B disease.

The immune response to the vaccine was short lived and it is not expected that anyone previously vaccinated would still have existing immunity to B disease. This programme was covered in previous editions of the *Handbook*.

Since this time there have been major advances in group B vaccine development, and there are now two recombinant group B vaccines (4CMenB and 2CMenB), both of which cover a broad range of group B subtypes. Neither vaccine is currently available in New Zealand.

The 4CMenB recombinant vaccine (Bexsero) contains four components from the group B bacteria: three different group B surface proteins plus detoxified outer membrane vesicles from the New Zealand group B epidemic strain. The 4CMenB vaccine has large-scale clinical trial data to support its use, and licensure has been granted in Europe, Australia, Canada and the US. The 4CMenB vaccine is associated with more local and febrile reactions than some other childhood vaccines. No serious adverse events have been identified; however, febrile seizures have occurred in temporal association with this vaccine.[9]

The 2CMenB recombinant vaccine (Trumenba) contains two group B surface proteins. One protein from each factor H binding protein subfamily (A and B) is included in the vaccine. The immunogenicity and safety of 2CMenB was assessed in individuals aged 10 years and older who received the vaccine in studies conducted in the US, Europe and Australia. The vaccine was licensed in the US in October 2014. The most commonly reported side effects by those who received the 2CMenB vaccine were pain at the injection site, fatigue, headache, joint pain and chills.[10]

In February 2015 the US Advisory Committee on Immunization Practices recommended that individuals aged 10 years or older at increased risk for meningococcal disease should receive meningococcal B vaccine (either 4CMenB or 2CMenB).[10] In June 2015, this recommendation was extended to include all adolescents and young adults aged 16–23 years (with a preferred age of 16–18 years), to provide short-term protection against most strains of serogroup B meningococcal disease.[11] In September 2015 the UK introduced the 4CMenB vaccine as part of a funded schedule for infants.[12] The vaccine is offered to infants at ages 2 and 4 months, with a booster at age 12 months.[13]

12.4.2 Efficacy and effectiveness

Meningococcal group C conjugate vaccines

The first national immunisation programme using a conjugate group C meningococcal vaccine was introduced in the UK in 1999. Group C conjugate vaccine was introduced into the UK infant immunisation schedule at ages 2, 3 and 4 months, as well as via a mass vaccination campaign up to age 20 years. Four years after introduction the overall reported effectiveness was at least 83 percent in children who had received the conjugate vaccine from age 5 months to 18 years.[14] Data from that programme indicates that a booster dose in the second year of life is important for sustained protection following infant vaccination.

The meningococcal C programme introduced in the UK in 1999 was successful in reducing invasive disease meningococcal C to a very small number of cases.[13] The routine schedule for protection against meningococcal C subsequently moved to a primary dose at age

12 months (as combined Hib-meningococcal C) and a booster at age 14 years (as MCV4).

Protective efficacy against carriage by adolescents of group C one year after the UK immunisation campaign was estimated at 69 percent.[15] At the same time there was no increase in colonisation by the other meningococcal groups. Consistent with the reduction in meningococcal carriage rates, there has been a 67 percent reduction in group C disease among unvaccinated children within the target age groups and a reduction of 35 percent of cases in unvaccinated adults older than age 25 years.[16] At the same time there was no evidence of capsular switching or an increase in disease caused by group B strains.[17]

The optimal vaccine schedule for sustained control of group C meningococcal disease by a universal programme has yet to be established. It is now recognised that circulating antibody is probably required for vaccine-induced protection and that antibody decay occurs quite rapidly in young children. Although conjugate vaccines can induce an anamnestic response, invasive disease develops within hours or days of acquisition and colonisation of the nasopharynx. This timeframe is shorter than that required for bactericidal antibodies to develop.

Herd protection, from reduced carriage resulting in reduced exposure to the organism, has an important role in the prevention of meningococcal disease. Consequently, further doses may be needed, possibly in early adolescence and then prior to leaving school. The exact timing will depend on any catch-up vaccination programme undertaken when the vaccine is first introduced, and the country's specific epidemiology.

Quadrivalent meningococcal conjugate vaccines

An estimate of the effectiveness of the diphtheria conjugate quadrivalent meningococcal vaccine (MCV4-D, Menactra) among adolescents in the US was determined as 80–85 percent, which is similar to that reported for the polysaccharide vaccines.[18] Estimates from a large case-control study in the US evaluating one of the two MCV4 vaccines, MCV4-D, suggest high vaccine effectiveness early after vaccination, but two to five years after vaccination, vaccine effectiveness wanes to 50–60 percent.[1]

The MCV4-D vaccine was poorly immunogenic in infants aged under 6 months,[19] and it is currently registered in New Zealand for individuals aged 9 months to 55 years.

The MCV4-T vaccine (Nimenrix) is registered in New Zealand for individuals aged 12 months to 55 years. Clinical trials showed that the vaccine was immunogenic in children above the age of 12 months, adolescents, and adults, and has an acceptable reactogenicity and safety profile.[20]

Although both conjugate quadrivalent meningococcal vaccines available in New Zealand are licensed up to age 55 years, there was no published data for evidence of the effectiveness in older adults identified at the time of writing.

Quadrivalent meningococcal polysaccharide vaccines

These are not currently available in New Zealand. Conjugated quadrivalent vaccines are used in preference to polysaccharide vaccines.

12.4.3 Transport, storage and handling

Transport meningococcal conjugate vaccines according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[21] Store at +2°C to +8°C. MCV4-D and MCV4-T should be protected from light. Do not freeze.

Reconstitution

MCV4-T (Nimenrix) must be reconstituted with the supplied diluent and used as soon as possible.

12.4.4 Dosage and administration

Meningococcal group C conjugate vaccine (MenCCV)

Each MenCCV (NeisVac-C) dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

For healthy infants aged under 12 months, two doses are given at least eight weeks apart, with the first dose given not earlier than age 8 weeks. A booster is given in the second year of life. For healthy children, adolescents and adults, one dose is given. See Table 12.5 for schedules for at-risk individuals.

MenCCV can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites.

Quadrivalent meningococcal conjugate vaccines (MCV4)

Each MCV4 dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

Menactra (MCV4-D)

Menactra is registered in New Zealand for individuals aged 9 months to 55 years. For healthy children aged 9–23 months, two doses are given at least three months apart. For healthy individuals aged 2–55 years, one dose is given. See Table 12.5 for schedules for at-risk individuals.

MCV4-D can be concurrently administered with other vaccines in separate syringes and at separate sites,[22, 23, 24, 25] except for PCV13. MCV4-D should be administered at least four weeks after PCV13. This is because when administered concurrently, there is impairment of the immune response to some of the pneumococcal serotypes.[26, 27]

Nimenrix (MCV4-T)

Nimenrix is registered in New Zealand for individuals aged 12 months to 55 years. One dose is given.

MCV4-T can be concurrently administered with other vaccines in separate syringes and at separate sites; however, there is no data on concurrent administration of MCV4-T and PCV13.

12.5 Recommended immunisation schedule

12.5.1 At-risk individuals

Meningococcal conjugate vaccines are not on the Schedule but are funded in special circumstances, as described in the shaded section of Table 12.4 below, with recommended dosing schedules in Table 12.5.

See sections 4.2 and 4.3 for more information about vaccination of special groups, including recommended immunisation schedules for high-risk individuals with certain medical conditions.

The conjugate vaccines are recommended (but not funded) for other individuals at risk, as described in Table 12.4.

Before travel

There are areas of the world where the risk of acquiring meningococcal infection is increased. Nevertheless, the risk to travellers to the developing world as a whole has been estimated as being less than one in a million per month. Recurrent epidemics of meningococcal disease occur in the sub-Saharan 'meningitis belt', from Senegal in the west to Ethiopia in the east, usually during the dry season (December to June). Epidemics are occasionally identified in other parts of the world and occurred recently in Saudi Arabia (during a Hajj pilgrimage), Kenya, Tanzania, Burundi, Mongolia and Nepal.

MCV4-D or MCV4-T are the preferred vaccines for travel. For website sources for information about meningococcal vaccines for travellers, see the WHO website (www.who.int/ith/en). Quadrivalent meningococcal vaccine is a requirement for pilgrims to the Hajj.

Before moving into communal living situations

Adolescents and young adults living, or planning to live, in communal accommodation such as a hostel, student accommodation, boarding school, in military accommodation, in correctional facilities or in other long-term institutions are likely to be at higher risk of acquiring meningococcal infection. Meningococcal vaccination should be considered.

Table 12.4: Meningococcal group C conjugate (MenCCV) and quadrivalent meningococcal vaccine (MCV4) recommendations

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Recommended and funded
MenCCV and MCV4-D are recommended and funded for: • patients pre- or post-splenectomy or with functional asplenia[a,b] • patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited) or who are pre- or post-solid organ transplant[b] • HSCT (bone marrow transplant) patients[b] • patients following immunosuppression[b,c] • close contacts of meningococcal cases[d]
Recommended but not funded
MenCCV, MCV4-D or MCV4-T are recommended, but not funded, for individuals: • who are laboratory workers regularly handling meningococcal cultures • who are adolescents and young adults living in communal accommodation (eg, in a hostel or at boarding school, in military accommodation, in correctional facilities or in other long-term institutions). MCV4-D or MCV4-T are recommended, but not funded, for individuals: • who are travelling to high-risk countries (see www.who.int/ith/en) or before the Hajj.

a Pneumococcal, Hib, influenza and varicella vaccines are also recommended for individuals pre- or post-splenectomy or with functional asplenia. See section 4.3.4.

b See sections 4.2 and 4.3 for more information.

c The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

d Only one dose is funded for close contacts of meningococcal cases.

Table 12.5: Recommended meningococcal vaccine schedule for high-risk individuals (funded)

Note: See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged 6 weeks to under 12 months	MenCCV (NeisVac-C) and	Age-appropriate MenCCV schedule: • if aged under 6 months at diagnosis, give 2 doses 8 weeks apart, with a booster at age 12 months • if aged 6–11 months at diagnosis, give 1 dose, with a further dose at age 12 months.
	MCV4-D (Menactra)	At age 2 years, give 2 doses of MCV4-D[a] 8 weeks apart, then a booster dose after 3 years, then 5-yearly.
Children aged 12 months to under 18 years	MenCCV (NeisVac-C) and MCV4-D (Menactra)	If aged 12–23 months at diagnosis, give 1 dose of MenCCV, followed by MCV4-D[a] at age 2 years, 2 doses 8 weeks apart; then a booster of MCV4-D after 3 years, then 5-yearly. If aged ≥2 years at diagnosis, give 2 doses of MCV4-D[a] 8 weeks apart, and: • if the 1st MCV4-D dose was given at age <7 years, give a booster after 3 years, then 5-yearly, or • if the 1st MCV4-D dose was given at age ≥7 years, give a booster dose every 5 years.
Adults aged 18 years and older	MCV4-D (Menactra)	Give 2 doses of MCV4-D, 8 weeks apart, then 1 dose every 5 years.[a,b]

a Give MCV4-D at least 4 weeks after PCV13.[26, 27]

b MCV4-D is registered for individuals aged 9 months to 55 years, but there are not expected to be any safety concerns when administered to adults older than 55 years.

12.5.2 Recommendations for children and adolescents

In the absence of a universal programme, non-high-risk children and adolescents may be offered meningococcal vaccines, but these are not funded. Table 12.6 suggests the most appropriate ages for this, reflecting the known ages of increased risk. The predominant meningococcal strains in New Zealand in childhood are B and C. There is no vaccine currently available in New Zealand for B. Particularly for those who are

likely to travel, the quadrivalent vaccine is preferable because of the differing serotype patterns between countries, for example, the Y serotype is prominent in the US.

Table 12.6: Suggested meningococcal vaccines for children and adolescents (not funded)

Note: Vaccine immunity is not long-lasting. The suggested ages of vaccination are not expected to protect individuals through all of childhood, but are pragmatically focused on offering protection during the ages of highest risk. This does not apply to epidemic situations.

Age	Vaccine options (trade name)	Number of doses
<12 months	MenCCV (NeisVac-C)	2 doses[a] (primary course) plus a booster after 12 months of age
12 months to 2 years	MenCCV (NeisVac-C), or MCV4-D (Menactra) or MCV4-T (Nimenrix)	1 MenCCV, or 2 MCV4-D[a,b] doses or 1 MCV4-T
Early adolescence (<16 years)	MenCCV (NeisVac-C) or MCV4-D (Menactra) or MCV4-T (Nimenrix)	1 dose plus a booster at age 16–18
Late adolescence ≥16 years	MenCCV (NeisVac-C) or MCV4-D (Menactra) or MCV4-T (Nimenrix)	1 dose, no booster required

a Refer to section 12.4.4 and the vaccine data sheets for the intervals between doses.

b MCV4-D should be administered at least 4 weeks after PCV13 (if used).[26, 27]

12.5.3 Pregnancy and breastfeeding

There are no reports of any adverse effects among pregnant women who have been vaccinated during pregnancy.[26] The vaccine may be given to pregnant women if indicated.[26] Meningococcal vaccine may be given to breastfeeding women.[28]

12.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

There are no specific contraindications for meningococcal vaccines, except for anaphylaxis to a previous dose or any component of the vaccine.

12.7 Expected responses and AEFIs

Frequent adverse reactions after meningococcal conjugate vaccines include localised pain, irritability, headache and fatigue.[2, 20] Fever is reported by 2 to 5 percent of adolescents who receive MCV4-D.

12.7.1 Meningococcal group C conjugate vaccine

The most frequent response to MenCCV in the UK school programme was transient headache in 12 percent of students in the first three days after vaccination.[29] This is more commonly reported by secondary students than primary school students. Mild to moderate local reactions at the injection site consisting of pain, tenderness and occasional redness were also reported. These peaked on the third day after the vaccine and resolved within a day.

A Cochrane Review assessed the safety of MenCCVs against group C disease.[30] MenCCVs were shown to have an excellent safety profile in infants. The events more frequently reported in infants were fever (1–5 percent), irritability (38–67 percent), crying more than expected (1–13 percent), redness at the site of vaccination (6–97 percent), tenderness at the site of vaccination (11–13 percent), and swelling at the site of vaccination (6–42 percent).

The adverse events were similar in groups vaccinated with MenCCV and with the hepatitis B control vaccine, but following booster doses they were more frequent in the MenCCV group in one trial. Adverse events were rare. Anaphylaxis was reported at a rate of one per 500,000 doses distributed.[29]

12.7.2 Quadrivalent meningococcal conjugate vaccine

The safety of two doses of MCV4-D was assessed in a phase III trial of infants: dose one was administered at age 9 months and dose two was administered at age 12 months, with or without routine childhood vaccines.[27] The percentage of participants with solicited systemic reactions after MCV4-D administration alone at age 12 months (60.6 percent) was lower than after the vaccination at age 9 months (68.2 percent), lower than the control groups at age 12 months (75.2–84.1 percent, depending upon the control vaccine), and lower than when

MCV4-D was administered concurrently with the routine childhood vaccines (68.3–73.2 percent).

The safety profile of MCV4-T (Nimenrix) is very similar to other meningococcal conjugate vaccines.[20]

Guillain–Barré syndrome

There is no evidence of an association between meningococcal conjugate vaccines and GBS.[28] An early report in the US of a suspected temporal association between MCV4-D (Menactra) and GBS was followed by a large retrospective cohort study in the US that found no evidence of an increased risk of GBS following administration of MCV4-D.[31, 32] If indicated, meningococcal conjugate vaccines may be administered to individuals with a history of GBS.[28]

12.8 Public health measures

Invasive meningococcal disease must be notified on suspicion to the local medical officer of health.

The overall rate of secondary cases in untreated adults is around 1 per 300. Adults and children in close contact with primary cases of invasive meningococcal infection are recommended to receive antibiotic prophylaxis, preferably within 24 hours of the initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

Blood or cerebrospinal fluid culture is the main diagnostic method, but blood PCR may be useful if antibiotics are given without prior access to blood culture. It is recommended that in primary care three to five millilitres of blood should be taken in an ethylenediaminetetraacetic acid (EDTA) anticoagulant tube (usually with a purple top) prior to administration of antibiotics unless blood culture is available. This should accompany the patient to hospital.

12.8.1 Contacts

A contact is anyone who has had unprotected contact with upper respiratory tract or respiratory droplets from the case during the seven days before onset of illness to 24 hours after onset of effective treatment.[33] Contacts at particular risk include:

- those sleeping at least one night in the same household, dormitory, military barrack, student hostel bunkroom (not residents of nursing or residential homes who sleep in separate rooms) as the case, or who have been in a seat adjacent to the case in a plane, bus or train for more than eight hours
- health care workers who have had intensive unprotected contact (not wearing a mask) with a case during intubation, resuscitation or close examination of the oropharynx
- exchange of upper respiratory tract secretions, including intimate kissing
- other contacts as determined by the medical officer of health on a case-by-case basis, such as children and staff attending an early childhood service.

Prophylaxis is not routinely recommended for health care personnel unless there has been intimate contact with oral secretions (eg, as a result of performing mouth-to-mouth resuscitation or suctioning of the case before antibiotic therapy has started).

12.8.2 Chemoprophylaxis for contacts

Recommended antibiotics

The recommended antibiotics are rifampicin, ceftriaxone or ciprofloxacin, preferably given within 24 hours of initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

Rifampicin

The recommended dose of rifampicin is 10 mg/kg (maximum dose 600 mg) every 12 hours for two days. For infants aged under 4 weeks, the recommended dose is 5 mg/kg every 12 hours for two days.

Avoid rifampicin if pregnant or breastfeeding.

Ceftriaxone

A single dose of intramuscular ceftriaxone (125 mg for children aged under 12 years and 250 mg for older children and adults) has been found to have an efficacy equal to that of rifampicin in eradicating the meningococcal group A carrier state. Ceftriaxone is the drug of choice in a pregnant woman because rifampicin is not recommended later in pregnancy. Ceftriaxone may be reconstituted with lignocaine (according to the manufacturer's instructions) to reduce the pain of injection. A New Zealand study demonstrated that ceftriaxone and rifampicin were equivalent in terms of eliminating nasopharyngeal carriage of *N. meningitidis* group B.[34]

Do not use in infants under aged under 4 weeks.

Ciprofloxacin

Ciprofloxacin given as a single oral dose of 500 mg or 750 mg is also effective at eradicating carriage. This is the preferred prophylaxis for women on the oral contraceptive pill and for prophylaxis of large groups.[33]

Ciprofloxacin is not generally recommended for pregnant and lactating women or for children aged under 18 years.[35] Consult the manufacturer's data sheet for appropriate use and dosage of ciprofloxacin in children.

Use of meningococcal conjugate vaccines for close contacts

Close contacts of cases of meningococcal disease may be offered the appropriate meningococcal conjugate vaccine (see section 12.5). See below for the use of the vaccines for the control of outbreaks, as initiated by the local public health service.

12.8.3 Outbreak control

When there is an outbreak of meningococcal disease of a specific vaccine group, an immunisation programme may be recommended and funded for a defined population. The local medical officer of health will determine the necessary action in discussion with the Ministry of Health.

For more details on control measures, refer to the '*Neisseria meningitidis* invasive disease' chapter of the *Communicable Disease Control Manual 2012*.[33]

12.9 Variations from the vaccine data sheets

The MCV4-D data sheet states that the vaccine is indicated for use in individuals aged 9 months to 55 years. The Ministry of Health recommends that this vaccine may be used in adults aged over 55 years.[28]

The data sheet states that MCV4-D should be given as a single dose for individuals aged 2 years and older. The Ministry of Health recommends that two doses are given to individuals at high risk of meningococcal disease (see Table 12.5 and section 4.3), with booster doses every five years (if the first MCV4-D was given before age 7 years, give a booster after three years, then five-yearly).[2]

A history of GBS is listed as a precaution in the MCV4-D data sheet. However, there is no evidence of an association between meningococcal conjugate vaccines and GBS (see section 12.7.2).[28] The Ministry of Health advises that, if indicated, MCV4-D may be administered to individuals with a history of GBS.[28]

The MenCCV data sheet states that the first dose of vaccine should not be given earlier than age 8 weeks. However, the Ministry of Health recommends that MenCCV may be given from age 6 weeks to infants at high risk of meningococcal disease (see Tables 12.4 and 12.5).

References

1. Cohn A, MacNeil J. 2015. The changing epidemiology of meningococcal disease. *Infectious Disease Clinics of North America* 29(4): 667–77. DOI: http://dx.doi.org/10.1016/j.idc.2015.08.002 (accessed 3 December 2016).

2. American Academy of Pediatrics. 2015. Meningococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, et al (eds). *Red Book: 2015 Report of the Committee on Infectious Diseases* (30th edition). Elk Grove Village, IL: American Academy of Pediatrics.

3. Meningococcal Disease Surveillance Group. 1976. Analysis of endemic meningococcal disease by serogroup and evaluation of chemoprophylaxis. *Journal of Infectious Diseases* 134(2): 201–4.

4. Neal KR, Nguyen-Van-Jam J, Jeffrey N, et al. 2000. Changing carriage rate of *Neisseria meningitidis* among university students during the first week of term: cross sectional study. *British Medical Journal* 320(7238): 846.

5. Bruce MG, Rosenstein NE, Capparella JM, et al. 2001. Risk factors for meningococcal disease in college students. *Journal of the American Medical Association* 286(6): 688–93.

6. Nelson SJ, Charlett A, Orr HJ, et al. 2001. Risk factors for meningococcal disease in university halls of residence. *Epidemiology and Infection* 126(2): 211–17.

7. Institute of Environmental Science and Research Ltd. 2016. *Notifiable Diseases in New Zealand: Annual Report 2015*. URL: https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf (accessed 16 November 2016).

8. Baker M, McNicholas A, Garrett N, et al. 2000. Household crowding a major risk factor for epidemic meningococcal disease in Auckland children. *Pediatric Infectious Diseases Journal* 19(10): 983–90.

9. Vesikari T, Esposito S, Prymula R, et al. 2013. Immunogenicity and safety of an investigational multicomponent, recombinant, meningococcal serogroup B vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomised trials. *The Lancet* 381(9869): 825–35.

10. Centers for Disease Control and Prevention. 2015. Use of serogroup B meningococcal vaccines in persons aged ≥10 years at increased risk for serogroup B meningococcal disease: recommendations of the Advisory Committee on Immunization Practices, 2015. *Mortality and Morbidity Weekly Report* 64(22): URL: http://www.cdc.gov/mmwr/pdf/wk/mm6422.pdf (accessed 25 August 2015).

11. Centers for Disease Control and Prevention. 2015. Use of serogroup B meningococcal vaccines in adolescents and young adults: recommendations of the Advisory Committee on Immunization Practices, 2015. *Morbidity and Mortality Weekly Report* 64(41): 1171–6. URL: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6441a3.htm (accessed 1 December 2016).

12. Public Health England. 2015. *Immunisation Against Meningococcal B Disease for Infants Aged from Two Months: Information for Health Professionals*. URL: https://www.gov.uk/government/publications/meningococcal-b-vaccine-information-for-healthcare-professionals (accessed 17 July 2015).

13. Public Health England. 2016. Meningococcal. In: *The Green Book*. URL: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/554011/Green_Book_Chapter_22.pdf (accessed 1 December 2016).

14. Campbell H, Borrow R, Salisbury D, et al. 2009. Meningococcal C conjugate vaccine: the experience in England and Wales. *Vaccine* 27(Suppl 2): B20–9.

15. Maiden MCJ, Stuart JM, for the UK Carriage Group. 2002. Carriage of serogroup C meningococci 1 year after meningococcal C conjugate polysaccharide vaccination. *The Lancet* 359(9320): 1829–31.

16. Ramsay ME, Andrews NJ, Trotter CL, et al. 2003. Herd immunity from meningococcal serogroup C conjugate vaccination in England: database analysis. *British Medical Journal* 326(7385): 365–6.

17. Balmer P, Borrow R, Miller E. 2002. Impact of meningococcal C conjugate vaccine in the UK. *Journal of Medical Microbiology* 51(9): 717–22.

18. MacNeil JR, Cohn AC, Zell ER, et al. 2011. Early estimate of the effectiveness of quadrivalent meningococcal conjugate vaccine. *Pediatric Infectious Disease Journal* 30(6): 451–5.

19. Rennels M, King J, Ryall R, et al. 2004. Dosage escalation, safety and immunogenicity study of four dosages of a tetravalent meningococcal polysaccharide diphtheria toxoid conjugate vaccine in infants. *Pediatric Infectious Disease Journal* 23(5): 429–35.

20. Hedari CP, Khinkarly RW, Dbaibo GS. 2014. Meningococcal serogroups A, C, W-135, and Y tetanus conjugate vaccine: a new conjugate vaccine against invasive meningococcal disease. *Infection and Drug Resistance* 7(3 April): 85–99. DOI: 10.2147/IDR.S36243 (accessed 25 August 2015).

21. Ministry of Health. 2017. *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*. URL: www.health.govt.nz/coldchain (accessed 14 February 2017).

22. Arguedas A, Soley C, Loaiza C, et al. 2010. Safety and immunogenicity of one dose of MenACWY-CRM, an investigational quadrivalent meningococcal glycoconjugate vaccine, when administered to adolescents concomitantly or sequentially with Tdap and HPV vaccines. *Vaccine* 28(18): 3171–9.

23. Gasparini R, Conversano M, Bona G, et al. 2010. Randomized trial on the safety, tolerability, and immunogenicity of MenACWY-CRM, an investigational quadrivalent meningococcal glycoconjugate vaccine, administered concomitantly with a combined tetanus, reduced diphtheria, and acellular pertussis vaccine in adolescents and young adults. *Clinical and Vaccine Immunology* 17(4): 537–44.

24. Bryant KA, McVernon J, Marchant CD, et al. 2012. Immunogenicity and safety of measles-mumps-rubella and varicella vaccines coadministered with a fourth dose of *Haemophilus influenzae* type b and *Neisseria meningitidis* serogroups C and Y-tetanus toxoid conjugate vaccine in toddlers: a pooled analysis of randomized trials. *Human Vaccines & Immunotherapeutics* 8(8): 1036–41.

25. Klein NP, Reisinger KS, Johnston W, et al. 2012. Safety and immunogenicity of a novel quadrivalent meningococcal CRM-conjugate vaccine given concomitantly with routine vaccinations in infants. *Pediatric Infectious Disease Journal* 31(1): 64–71.

26. Centers for Disease Control and Prevention. 2013. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report: Recommendations and Reports* 62(2): 1–28. URL: www.cdc.gov/mmwr/pdf/rr/rr6202.pdf (accessed 27 September 2013).

27. Pina LM, Bassily E, Machmer A, et al. 2012. Safety and immunogenicity of a quadrivalent meningococcal polysaccharide diphtheria toxoid conjugate vaccine in infants and toddlers: three multicenter phase III studies. *Pediatric Infectious Disease Journal* 31(11): 1173–83.

28. Department of Health and Ageing. 2016. Meningococcal disease. In: *The Australian Immunisation Handbook* (10th edition; updated August 2016). URL: http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-10 (accessed 21 December 2016).

29. Granoff DM, Pelton S, Harrison LH. 2013. Meningococcal vaccines. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders.

30. Conterno LO, da Silva Filho CR, Ruggeberg JU, et al. Conjugate vaccines for preventing meningococcal C meningitis and septicaemia (Review). *Cochrane Database of Systematic Reviews* 2006, Issue 3, Art. No. CD001834. DOI: 10.1002/14651858.CD001834.pub2 (accessed 20 August 2013).

31. Centers for Disease Control and Prevention. 2013. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Mortality and Morbidity Weekly Report Recommendations and Reports* 62(RR 02): 1-28.

32. Velentgas P, Amato AA, Bohn RL, et al. 2012. Risk of Guillain-Barré syndrome after meningococcal conjugate vaccination. *Pharmacoepidemiology and Drug Safety* 21(12): 1350–8. DOI: 10.1002/pds.3321 (accessed 21 December 2016).

33. Ministry of Health. 2012. *Communicable Disease Control Manual 2012*. URL: http://www.health.govt.nz/publication/communicable-disease-control-manual-2012 (accessed 15 November 2016).

34. Simmons G, Jones N, Calder L. 2000. Equivalence of ceftriaxone and rifampicin in eliminating naso-pharyngeal carriage of serogroup B *N. meningitidis*. *Journal of Antimicrobial Chemotherapy* 45(6): 909–11.

35. Schaad UB, Salam MA, Aujard Y, et al. 1995. Use of fluoroquinolones in pediatrics: consensus report of an International Society of Chemotherapy Commission. *Pediatric Infectious Disease Journal* 14(1): 1–9.