

Meningococcal disease

MENINGOCOCCAL VACCINES FOR AUSTRALIANS: INFORMATION FOR IMMUNISATION PROVIDERS

Disease and epidemiology

- Meningococcal disease is rare but serious. Septicaemia and/or meningitis are the most common clinical manifestations of invasive meningococcal disease.
- Meningococcal disease is caused by the bacterium *Neisseria meningitidis*. There are 13 serogroups; those that most commonly cause disease are A, B, C, W₁₃₅ and Y.
- The incidence of meningococcal disease fluctuates naturally over time. The total notification rate of invasive meningococcal disease has declined since 2001. A natural decrease in disease caused by serogroup B, the predominant serogroup in Australia, has also occurred.
- In Australia in recent years, serogroup B was the cause of approximately 85% of meningococcal disease (where the serogroup was known).
- The conjugate meningococcal C vaccine was introduced to the National Immunisation Program (NIP) in 2003. Since 2004, there has been a significant and sustained reduction in serogroup C meningococcal cases.

Vaccines

- Four types of meningococcal vaccines are registered in Australia:
 - (1) meningococcal C conjugate vaccines (MenCCV), also available in a combination formulation with the *Haemophilus influenzae* type b (Hib) vaccine (Hib–MenCCV)
 - (2) multicomponent meningococcal B vaccine (MenBV)
 - (3) quadrivalent (A, C, W₁₃₅, Y) meningococcal conjugate vaccines (4vMenCV)
 - (4) quadrivalent (A, C, W₁₃₅, Y) meningococcal polysaccharide vaccines (4vMenPV).

Who should be vaccinated

- A single dose of MenCCV is recommended for all children at 12 months of age. This is available through the NIP as the combination Hib–MenCCV vaccine. Children aged ≥12 months and adolescents who missed receiving a dose of MenCCV previously should receive a catch-up dose. Additional doses are recommended for those with complement disorders, asplenia and other immunocompromising conditions.
- MenBV can be given to individuals 6 weeks of age or older and is recommended for use in those with increased risk of invasive meningococcal disease because of age, medical conditions or occupational exposure. It is not currently funded under the NIP.
- Routine vaccination with quadrivalent meningococcal vaccines is not recommended. However, vaccination is recommended for individuals with increased risk of disease due to complement disorders, asplenia and other immunocompromising conditions, or exposure due to occupation or travel. In most circumstances, use of 4vMenCV is preferred over 4vMenPV.

The disease

Meningococcal disease is caused by the bacterium *Neisseria meningitidis*, commonly known as the meningococcus. There are 13 serogroups, distinguished by differences in the surface polysaccharides of the outer membrane capsule. Globally, most meningococcal disease is caused by serogroups A, B, C, W₁₃₅ and Y.

Meningococcal disease is relatively rare but is very often serious. Septicaemia, meningitis or a combination of both are the most common manifestations of invasive meningococcal disease (defined by isolation of meningococci from sites that are normally sterile). Today, even with antibiotic treatment, the mortality risk is approximately 5–10%. Furthermore, about 10–30% of children and adolescents who survive the disease develop permanent sequelae such as limb deformity, skin scarring, deafness and neurological deficits.^{1–3} Other less common manifestations of meningococcal disease include pneumonia, arthritis, epiglottitis, pericarditis and conjunctivitis.^{4–6} Primary meningococcal conjunctivitis may precede invasive disease.⁷

Clinical features

The symptoms of meningococcal septicaemia and meningitis may not necessarily be typical and are often non-specific. They can include sudden onset of fever, a rash that can be petechial or purpuric (i.e. like red-purple spots or bruises) or maculopapular, headache, neck stiffness, photophobia, altered consciousness, muscle aches, cold hands, thirst, joint pain, nausea and vomiting.^{1,4,5,8}

Not all symptoms or signs may be present at disease onset. The characteristic rash of meningococcal disease (a rash which does not disappear with gentle pressure on the skin) is not always present.

Transmission

Meningococci are carried and transmitted only by humans. Individuals within a population who are not unwell can carry meningococci in their throat and/or nose. The prevalence and duration of carriage varies over time and in different populations and age groups. For example, studies show prevalence of carriage increases from 4.5% in infants to a peak of 23.7% in adolescents, and then decreases in adulthood to 7.8% in 50-year olds.⁹

Meningococcal bacteria are transmitted in respiratory droplets. The risk of acquiring infection is increased by regular, prolonged close contact such as living in the same household or intimate kissing.

The disease has an incubation period of 1–10 days, most commonly 3–4 days.

Risk factors for acquiring the disease

Individuals who are immunocompromised due to certain disorders of the immune system (particularly complement deficiencies), certain medical treatments, or functional or anatomical asplenia have an increased risk of acquiring the disease.

Other risk factors for meningococcal infection include occupational exposure to meningococci in microbiological laboratories, exposure to smokers (who are more likely to be carriers), crowded living conditions, intimate kissing with multiple partners, and recent or current viral infection of the upper respiratory tract.^{4,8}

Management of meningococcal disease

Invasive meningococcal disease is notifiable in all states and territories and prompt diagnosis and medical treatment is important. If meningococcal disease is suspected, the patient should be treated promptly with appropriate parenteral antibiotics and referred to hospital for further emergency clinical management. The relevant state/territory public health authority should be notified as soon as possible so that contacts can be identified and the appropriate public health response determined in accordance with national guidelines.¹⁰ This may include vaccination (see [Use of vaccines for close contacts...](#)).

Epidemiology

Meningococci cause both sporadic and epidemic disease throughout the world, but the dominant serogroup(s) varies geographically. Serogroup A disease occurs predominantly in low-income countries, particularly countries in sub-Saharan Africa. Meningococcal serogroup B ('MenB') is the major cause of sporadic meningococcal disease in many developed countries. In Australia, MenB has been the predominant serogroup even before, but particularly since, the meningococcal C ('MenC') conjugate vaccine program began in 2003. In the two years of 2012–2013, there were 333 cases of laboratory-confirmed invasive meningococcal disease in which the serogroup could be determined (95% of 351 laboratory-confirmed cases). Of these cases, about 80% were due to MenB. The remainder were due to serogroup C (about 6%), serogroup W₁₃₅ (6%) and serogroup Y (9%).^{11,12}

In Australia meningococcal disease follows a seasonal trend, with most cases occurring in winter or early spring.^{11,13} Most meningococcal disease occurs in young children <5 years of age and in older adolescents/young adults (15–24 years of age).¹³ The highest incidence of MenB disease is in children aged <5 years (5.7 cases per 100,000 in 2006–2011), particularly infants aged <1 year (14.0 cases per 100,000). There is also a lower, secondary

peak in late adolescence and early adulthood (2.8 cases per 100,000 aged 15–19 years) (Table 1). In comparison, the peak incidence of meningococcal C disease in Australia in 1999–2002, prior to the MenC vaccination program, was in late adolescence (3.3 cases per 100,000 aged 15–19 years) with a lower peak in children aged <5 years (2.3 per 100,000).

Table 1. Case numbers and notification rates for MenB disease in Australia, by age

Age group	Annual average case counts (2006–2011)	Annual average notification rate (per 100,000) (2006–2011)
<1 year	40	14.0
1 year	18	6.3
2–4 years	21	2.6
5–14 years	21	0.7
15–19 years	41	2.8
20–24 years	19	1.2
≥25 years	45	0.3
Total annual average	204	0.95

Data source: National Notifiable Diseases Surveillance System

The incidence of meningococcal disease fluctuates naturally over time so there are periods of higher and lower incidence of the disease. In Australia, notification rates of meningococcal disease have been decreasing in the past decade, from the peak of 3.5 cases per 100,000 in 2001 to 1.1 per 100,000 in 2011. This was not just attributable to the decline in MenC incidence following the implementation of the national MenC conjugate vaccination program in 2003; MenB incidence also declined substantially.¹³ There is no clear explanation for why this has occurred and the future trend cannot be predicted.

Vaccines

There is no single vaccine that offers protection against all serogroups that cause meningococcal disease. There are four types of meningococcal vaccines, covering different serogroups, registered in Australia:

- 1) meningococcal C conjugate vaccines (MenCCV)
- 2) multicomponent meningococcal B vaccine (MenBV)
- 3) quadrivalent meningococcal conjugate vaccines (4vMenCV)
- 4) quadrivalent meningococcal polysaccharide vaccines (4vMenPV).

Meningococcal C conjugate vaccines (MenCCV)

In MenCCVs, the serogroup C antigen is conjugated to a carrier protein. The use of this vaccine in population vaccination programs has resulted in marked reductions in MenC invasive disease in the eligible age groups in the UK (reduced by up to 97%)¹⁴ and in other countries.¹⁵ Indirect protective benefits ('herd immunity') have also been shown in other age groups who were not vaccinated.¹⁵ Similar effects have been seen in Australia.

For children aged 12 months or older, a single dose of MenCCV-containing vaccine is sufficient to induce a strong protective antibody response.¹⁶ Although waning of antibody levels has been observed,^{17–19} current MenC epidemiology^{12,13} in Australia suggests protection following vaccination is ongoing and that booster doses are not required.¹⁶

Since July 2013, a combination formulation of meningococcal C conjugate and *Haemophilus influenzae* type b vaccines (Hib–MenCCV), **Menitorix**[®] (GlaxoSmithKline), has replaced the two separate vaccines on the National Immunisation Program (NIP) schedule at 12 months of age.

The monovalent meningococcal C conjugate vaccines that have been registered for use in Australia are **Meningitec**[®] (Emerge Health), **Menjugate**[®] **Syringe** (bioCSL/Novartis) and **NeisVac-C**[®] (Baxter).

Multicomponent meningococcal B vaccine (MenBV)

MenBV (**Bexsero**[®], Novartis) is a recombinant multicomponent vaccine designed to provide protection against MenB. It was registered in Australia in August 2013. It contains four major antigens that are highly conserved across multiple MenB strains. Based on laboratory tests, it is estimated that the vaccine induces protective antibodies against about 75% of MenB strains in Australia.²⁰ This vaccine differs from other MenB vaccines used in other countries, for example New Zealand, for control of epidemics dominated by a single MenB strain.²¹

The clinical efficacy of MenBV cannot feasibly be assessed in clinical trials as invasive MenB disease is rare. Instead, the immunogenicity of this vaccine has been demonstrated through laboratory methods that correlate with protection against clinical meningococcal disease. There is currently a lack of data to inform the duration of protection of MenBV and the immunogenicity of MenBV in people who are immunocompromised.

The primary vaccination course of MenBV consists of 2–4 doses, depending on the age at which the course commences. Refer to *The Australian Immunisation Handbook*, 10th edition, 2015 update, for more details.¹⁶

MenBV may be administered concurrently, at separate injection sites, with other infant vaccines in the NIP schedule. However, concurrent administration of MenBV with other vaccines will increase the frequency of vaccine-related adverse reactions, most notably fever, compared to when MenBV or other vaccines are administered on their own. Due to this concern, the prophylactic use of paracetamol is recommended with every dose of MenBV for children <2 years of age (see [Vaccine safety](#)).

Individuals who have previously received other meningococcal vaccines (including the strain-specific meningococcal B vaccine previously used in New Zealand) can receive MenBV.

Quadrivalent meningococcal conjugate vaccines (4vMenCV)

In 4vMenCVs, the antigens of four serogroups (A, C, W₁₃₅ and Y) are conjugated to a carrier protein. Several clinical trials have demonstrated the immunogenicity of 4vMenCV in adolescents, young adults and children. All studies indicate that 4vMenCVs are safe and immunogenic.²²

Unlike quadrivalent polysaccharide vaccines (i.e. without protein conjugation), conjugate vaccines are immunogenic in young infants, induce a greater antibody response (especially in younger children), and induce a T cell-dependent immune response and immunological memory.

The 4vMenCVs registered for use in Australia are **Menactra**[®] (Sanofi Pasteur), **Menveo**[®] (bioCSL/Novartis) and **Nimenrix**[®] (GlaxoSmithKline).

Routine vaccination with 4vMenCV is not recommended on a population level. However, certain groups at increased risk of disease due to occupational or travel disease exposure or medical conditions are recommended to be vaccinated (see [Who should be vaccinated](#)).

Quadrivalent meningococcal polysaccharide vaccines (4vMenPV)

4vMenPVs contain polysaccharide from four serogroups (A, C, W₁₃₅ and Y), but the antigens are not conjugated to a carrier protein as they are in 4vMenCVs.

4vMenPVs induce antibodies within 10–14 days of vaccination in about 90% of recipients aged >2 years. However, there is little response to the serogroup C component of 4vMenPV before 18 months of age and

little response to serogroup A before 3 months of age.²³ Also, as there is no protein carrier, this vaccine is unable to induce T cell-dependent immunity and immune memory. Immunity decreases during the first few years following a single dose, particularly in infants and young children. However, clinical protection persists for at least 3 years in school-aged children and adults.

An additional concern is the possibility of a blunted immune response (immunological hyporesponsiveness) to the vaccine serogroup(s) with subsequent dose(s) of meningococcal vaccines following receipt of a meningococcal polysaccharide vaccine. This has been demonstrated to occur, at least with the serogroup C component, in both children and adults.

Due to these considerations, the use of 4vMenCV is preferred over 4vMenPV where indicated (see [Who should be vaccinated](#)). However, 4vMenPV is a suitable alternative when the need for repeat doses is not anticipated.

The 4vMenPVs registered for use in Australia are **Mencevax**[®] **ACWY** (GlaxoSmithKline) and **Menomune**[®] (Sanofi Pasteur).

Who should be vaccinated

For detailed information about recommendations and use of meningococcal vaccines, please refer to Chapter 4.10 ‘Meningococcal disease’ in *The Australian Immunisation Handbook*, 10th edition, 2015 update.¹⁶

A summary of the meningococcal vaccines registered for use in Australia can be found in [Table 2](#).

Healthy infants and younger children

- A single dose of MenCCV is recommended for all children at the age of 12 months, provided through the NIP. Since July 2013, it is given in a combination formulation with the Hib vaccine (Hib–MenCCV).
- Healthy children who missed receiving a dose of MenCCV at 12 months of age, or received their last dose aged <12 months, should receive a catch-up dose.
- MenBV is recommended for infants and young children, particularly those aged <2 years.

Healthy adolescents

- Healthy adolescents who missed receiving a dose of MenCCV in childhood should receive a catch-up dose.
- A 2-dose schedule of MenBV is recommended for all adolescents aged 15–19 years. It is particularly recommended for those living in close conditions such as residential accommodation or military recruits.

Laboratory personnel who frequently handle *Neisseria meningitidis*

- A single primary dose of 4vMenCV is recommended. Those with ongoing occupational exposure risks should receive 4vMenCV boosters every 5 years, until further information regarding duration of immunity afforded by 4vMenCV becomes available.
- A primary course of 2 doses of MenBV (1–2 months apart) is also recommended.

Travellers

- A single primary dose of 4vMenCV is recommended for individuals (aged ≥2 months) who intend to travel to parts of the world where epidemics of group A, C, W₁₃₅ or Y disease are frequent.
- A single primary dose of 4vMenCV is recommended for pilgrims attending the annual Hajj (certificate of vaccination is a condition of entry to Saudi Arabia for this purpose).

The appropriate vaccine formulations and the required doses, including the need for a booster dose, differ by age. Refer to *The Australian Immunisation Handbook*, 10th edition, 2015 update, for more details.¹⁶

Those with medical conditions associated with increased risk of meningococcal disease

Additional doses of 4vMenCV and MenBV are recommended for individuals with medical conditions associated with an increased risk of meningococcal disease. These conditions include inherited defects or deficiency of properdin or complement components, current or future treatment with eculizumab, functional or anatomical asplenia, HIV infection, and haematopoietic stem cell transplant.

The appropriate vaccine formulations and the required doses, including the need for a booster dose, differ by age. Refer to *The Australian Immunisation Handbook*, 10th edition, 2015 update, for more details.¹⁶

Table 2. Meningococcal vaccines registered for use in Australia and groups recommended for vaccination

Trade name	Formulation	Provides protection against serogroup:					Population group recommended for vaccination (see also Who should be vaccinated)
		A	B	C	W ₁₃₅	Y	
Meningococcal C conjugate vaccines (MenCCV)							
Menitorix®	Hib–MenC conjugate combination vaccine			✓			All children, to be given at age 12 months. (All adolescents should have been vaccinated.) Monovalent vaccine replaced by Hib–MenCCV combination vaccine for use under NIP since July 2013.
		Also serves as a booster dose of Hib vaccine					
Meningitec®	MenC–CRM ₁₉₇ conjugate			✓			
Menjugate® Syringe	MenC–CRM ₁₉₇ conjugate			✓			
NeisVac-C®	MenC–tetanus toxoid conjugate			✓			
Multicomponent meningococcal B vaccine (MenBV)							
Bexsero®	Recombinant multicomponent MenB		✓*				Infants, adolescents and others at higher risk of MenB disease.
Quadrivalent meningococcal conjugate vaccines (4vMenCV)							
Menactra®	Quadrivalent diphtheria toxoid conjugate	✓		✓	✓	✓	Those with increased medical, occupational or other exposure (including travel) risks of meningococcal disease caused by serogroups contained in these vaccines.
Menveo®	Quadrivalent CRM ₁₉₇ conjugate	✓		✓	✓	✓	
Nimenrix®	Quadrivalent tetanus toxoid conjugate	✓		✓	✓	✓	
Quadrivalent meningococcal polysaccharide vaccines (4vMenPV)							
Mencevax® ACWY	Quadrivalent polysaccharide	✓		✓	✓	✓	Those with occupational or travel risk of meningococcal disease caused by serogroups contained in these vaccines. However, 4vMenCV is preferred, particularly in children aged <7 years and travellers of any age who anticipate ongoing or periodic travel-related exposure risk. 4vMenPV is suitable, however, when the need for repeat doses is not anticipated.
Menomune®	Quadrivalent polysaccharide	✓		✓	✓	✓	

* Bexsero® protects against MenB disease. There are many strains of serogroup B meningococcus. Bexsero® is estimated to protect against 76% of MenB strains in Australia.²⁰

Vaccine safety

Meningococcal conjugate vaccines

Meningococcal conjugate vaccines are generally considered safe and well tolerated. Common adverse events following MenCCV include pain, tenderness and occasional erythema at the injection site, which tend to be of mild to moderate severity and typically resolve within 1 day. Transient headache may also occur. However, serious adverse reactions are rare.⁴

The most frequently reported adverse events following 4vMenCV include fever, headache, dizziness²⁴ and erythema at the injection site. Injection site reactions generally resolve within 48–72 hours.⁴

Multicomponent meningococcal B vaccine

Fever was the most notable systemic reaction in infants and young children in clinical trials for MenBV. Concurrent administration of MenBV with other childhood immunisations has been shown to increase the frequency of fever,^{25,26} as shown in [Table 3](#).

Table 3. Proportion (%) of infants reporting fever within 7 days after at least 1 of the 3 infant doses²⁶

Axillary temperature	Routine vaccines alone	MenBV alone	Routine + MenBV
≥38°C	23–36%	26–41%	51–62%
≥39°C	3–4%	4–8%	10–15%

This increased likelihood of fever in infants can be reduced by prophylactic use of paracetamol (see [Box](#)). A clinical trial demonstrated that prophylactic use of paracetamol reduced the likelihood of high-grade fever by approximately half with no overall impact on immunogenicity of MenBV or the other vaccines given concurrently.²⁷

Prophylactic use of paracetamol with MenBV vaccination in children aged <2 years

Prophylactic use of paracetamol is recommended with every dose of MenBV administered to children <2 years of age. This is an exception to the general recommendation not to routinely give paracetamol with vaccinations unless it is for relief of fever or pain following immunisation – refer to *The Australian Immunisation Handbook*, 10th edition, 2015 update (Chapter 2.3).¹⁶

Other common adverse events following immunisation with MenBV include tenderness, swelling and erythema at the injection site, irritability, sleepiness, change in eating habits, unusual crying, rash, vomiting and diarrhoea. While these reactions were reported more frequently when MenBV was co-administered with other vaccines, most of these events were considered mild or moderate and were transient in nature. (Refer to *The Australian Immunisation Handbook*, 10th edition, 2015 update, for further details on adverse events.¹⁶)

Meningococcal polysaccharide vaccines

Injection site reactions following 4vMenPVs include pain and erythema, which are typically mild and last for 1 or 2 days. Transient low-grade fever has been reported in <5% of adult recipients, and severe systemic reactions are infrequent.⁴

Use of vaccines for close contacts of patients or in public health management of meningococcal disease outbreaks

The meningococcal vaccine with coverage of the relevant serogroup may be considered for individuals who have had close household or household-like contact with someone who has meningococcal disease, or for individuals at increased risk of disease because of a local disease outbreak (such as an outbreak in a residential facility). The relevant state/territory public health authority should be contacted as soon as possible for advice on determining the risk of disease and whether to offer vaccination (in addition to clearance antibiotics) and for guidance on management. (See also [Management of meningococcal disease](#).)

Contraindications/precautions

For all meningococcal vaccines (MenCCV/Hib–MenCCV, MenBV, 4vMenCV and 4vMenPV), the absolute contraindications are anaphylaxis following a previous dose of the respective vaccine, or anaphylaxis following any component of the vaccine. Previous meningococcal disease, regardless of the serogroup, is not a contraindication for vaccination.¹⁶

Additional resources for primary medical care/vaccination providers

- *The Australian Immunisation Handbook*, 10th edition – the most up-to-date clinical recommendations are contained in the online version of the *Handbook* www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home
- Immunise Australia website www.immunise.health.gov.au
- National Immunisation Program schedule www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule
- Centers for Disease Control and Prevention. Meningococcal disease. www.cdc.gov/meningococcal/

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