

# 22

## Meningococcal

### MENINGOCOCCAL MENINGITIS AND SEPTICAEMIA NOTIFIABLE

#### The disease

Meningococcal disease occurs as a result of a systemic bacterial infection by *Neisseria meningitidis*.

Meningococci are gram-negative diplococci, divided into antigenically distinct serogroups. They are classified according to characteristics of the polysaccharide capsule into capsular group, and of outer membrane proteins into type and subtype. Further characterisation, undertaken by sequencing several other regions of the chromosomal DNA, defines the sequence type (ST).

There are to date 12 identified capsular groups, A, B, C, E, H, I, K, L, W, X, Y, and Z, of which groups B, C, W and Y were historically the most common in the UK. However, since the introduction of the routine meningococcal C conjugate vaccination programme, cases of invasive meningococcal disease in the UK from serogroup C have reduced dramatically, with serogroup B now accounting for the vast majority of cases.

Meningococci colonise the nasopharynx of humans and are frequently harmless commensals. Between 5 and 11% of adults and up to 25% of adolescents carry the bacteria without any signs or symptoms of the disease. In infants and young children, the carriage rate is low (Christensen *et al.*, 2010). It is not fully understood why disease develops in some individuals but not in others. Age, season, smoking, preceding influenza A infection and living in 'closed' or 'semi-closed' communities, such as university halls of residence or military barracks, have been identified as risk factors (Cartwright, 1995).

Transmission is by aerosol, droplets or direct contact with respiratory secretions of someone carrying the organism. Transmission usually requires either frequent or prolonged close contact. There is a marked seasonal variation in meningococcal disease, with peak levels in the winter months declining to low levels by late summer.



Figure 22.1 The 'glass' test (picture courtesy of Meningitis Research Foundation)

Meningococcal infection most commonly presents as either meningitis or septicaemia, or a combination of both. Less commonly, individuals may present with pneumonia, myocarditis, endocarditis, pericarditis, arthritis, conjunctivitis, urethritis, pharyngitis and cervicitis (Rosenstein *et al.*, 2001).

The incubation period is from two to seven days and the onset of disease varies from fulminant with acute and overwhelming features, to insidious with mild prodromal symptoms. Early symptoms and signs are usually malaise, pyrexia and vomiting. Headache, neck stiffness, photophobia, drowsiness or confusion and joint pains may occur variably. In meningococcal septicaemia, a rash may develop, along with signs of advancing shock and isolated limb and/or joint pain. The rash may be non-specific early on but as the disease progresses the rash may become petechial or purpuric and may not blanch. This can readily be confirmed by gentle pressure with a glass (the 'glass test') when the rash can be seen to persist (Figure 22.1). In young infants particularly, the onset may be insidious and the signs may be non-specific without 'classical' features of meningitis.

Health professionals should be alert to the possibility of meningococcal infection in a young child presenting with vomiting, pyrexia and irritability and, if still patent, raised anterior fontanelle tension. Clinical deterioration may

be very rapid with poor peripheral perfusion, pallor, tachypnoea, tachycardia and the emergence of the meningococcal rash. In severe cases, patients may present with hypotension or in coma.

The incidence of meningococcal disease is highest in children under five years of age, with a peak incidence in those under one year of age. There is a secondary peak in incidence in young people aged 15 to 19 years of age.

The average annual incidence of invasive meningococcal disease across all age groups is 2 per 100,000 (Ladhani *et al.*, 2012). Overall case-fatality ratio in the UK fell from an historic average of 10% to reach 5% by 2011 (Ramsay *et al.*, 1997; Goldacre *et al.*, 2003; Ladhani *et al.*, 2012). Case-fatality ratio is higher in cases with septicaemia than in those with meningitis alone (Stanton *et al.*, 2011), increases with age, and are higher in individuals with serogroup C than serogroup B infections (Ramsay *et al.*, 1997). Some specific strains of *N. meningitidis* appear to be associated with higher case fatality ratios, even after controlling for age (Trotter *et al.*, 2002; Goldacre *et al.*, 2003). Studies in paediatric intensive care settings have indicated that prompt and active management may reduce fatality ratios (Thorburn *et al.*, 2001; Booy *et al.*, 2001). In those who survive, approximately 25% may experience a reduced quality of life, with 10–20% developing permanent sequelae (Erickson *et al.*, 1998; Granoff *et al.*, 2008). The most common long-term effects are skin scars, limb amputation(s), hearing loss, seizures and brain damage (Steven *et al.*, 1995; Granoff *et al.*, 2008).

## History and epidemiology of the disease

In the UK, large epidemics of meningococcal disease, probably caused by serogroup A infections, coincided with each of the two world wars (Figure 22.2) (Jones, 1995). After the Second World War, incidence declined. However, between 1972 and 1975, incidence increased temporarily, associated with a serogroup B serotype 2a strain. In 1985, another hyperendemic period began, associated with increased circulation of a hypervirulent ST32, B15:P1.16 strain. A further hyperendemic period started in 1995–96, associated with an increased proportion of disease due to ST11 serogroup C serotype 2a infection. There was a shift in age distribution towards teenagers and young adults, among whom case fatality ratios are particularly high.

Meningococcal disease occurs in all countries. In the ‘meningitis belt’ of sub-Saharan Africa, the incidence of meningococcal infection rises sharply towards the end of the dry, dusty season when disease spreads rapidly, resulting in large epidemics within very short periods. These are predominantly due to serogroup A, but recent outbreaks have included serogroups W and X.

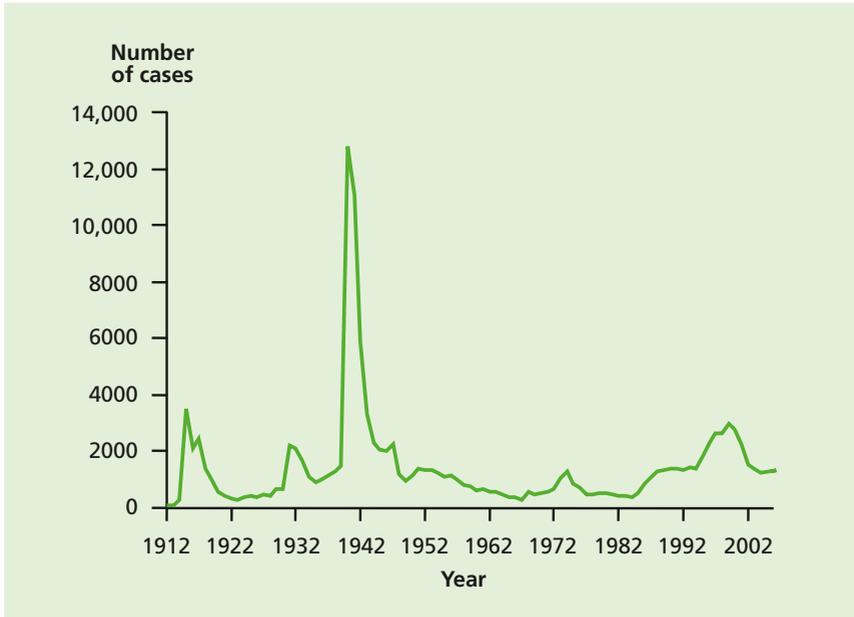


Figure 22.2 Notifications of meningococcal disease, England and Wales 1912–2004

Increasing numbers of countries in sub-Saharan countries have already introduced Group A meningococcal conjugate vaccine into routine and catch-up vaccination campaigns.

Large epidemics of meningococcal disease have been linked to the annual Hajj pilgrimage to Mecca in Saudi Arabia, resulting in importations into a number of countries, including the UK. These were initially caused by serogroup A infection and immunisation against this strain became a requirement for entry to Saudi Arabia. In 2000 and 2001, an increase in serogroup W infections followed the Hajj with a number of cases in UK pilgrims and their families (Hahne *et al.*, 2002). Evidence of receipt of quadrivalent vaccine (serogroups A, C, Y, W) became an entry requirement in 2002.

Meningococcal vaccines based solely on the serogroup C polysaccharide (often called ‘plain’ polysaccharide vaccines) provide only short-term protection to older children and adults and do not protect infants. In the mid-1990s, meningococcal C (MenC) conjugate vaccines were therefore

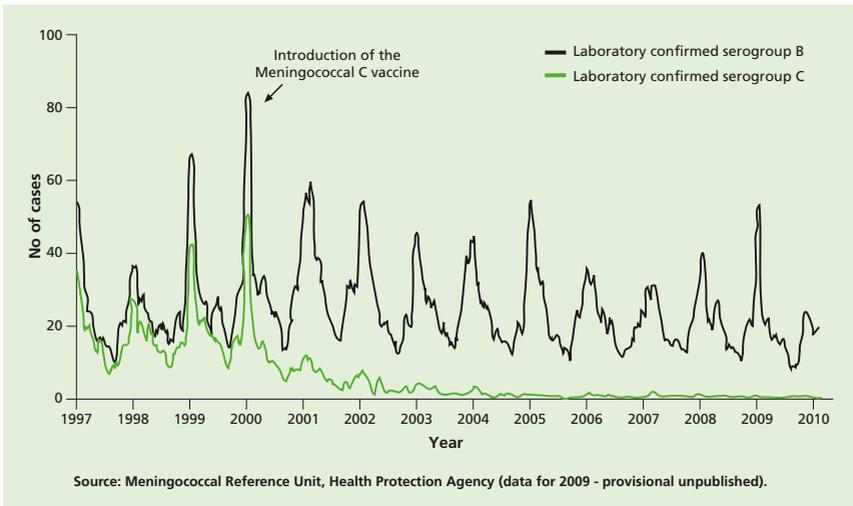


Figure 22.3 Laboratory-confirmed cases of meningococcal disease, England and Wales, five weekly moving averages. 1997 to 2009.

developed that would provide longer-term protection and would be effective in infants. As the rate of meningococcal serogroup C infections continued to rise, the development of the new vaccines was accelerated.

In November 1999, MenC conjugate vaccine was introduced into the UK routine immunisation programme along with a catch-up campaign for older children, adolescents and young adults up to 18 years. In January 2002, the campaign was extended to include adults under 25 years of age.

Following the MenC vaccine campaign, the number of laboratory-confirmed serogroup C cases fell by over 90% in all age groups immunised (Figure 22.3) (Campbell H, *et al.*, 2010; Miller *et al.*, 2001; Trotter *et al.*, 2004). Cases in other age groups fell by approximately two-thirds as a result of reduced carriage rates (Maiden *et al.*, 2002) and reduced risk of exposure (Trotter *et al.*, 2003). This indirect protection (or herd immunity) has contributed to the number of cases falling and remaining at very low levels.

In 2006, following studies that showed that protection against meningococcal serogroup C waned during the second year of life (Trotter *et al.*, 2004), a booster dose (combined with Hib vaccine as Hib/MenC vaccine) was introduced at 12 months of age.

In 2013, despite continuing excellent disease control, increasing evidence showed that vaccination against meningococcal serogroup C disease in early childhood provides short-term protective immune responses (Borrow *et al.*, 2010; Kitchen *et al.*, 2009; Perret *et al.*, 2010), that vaccination later in childhood provides higher levels of antibodies that persist for longer (Snape *et al.*, 2008), and that meningococcal serogroup C vaccination significantly reduced nasopharyngeal carriage of serogroup C meningococcus providing indirect protection through herd protection (Ramsay *et al.*, 2003; Maiden *et al.*, 2008). This led the JCVI to consider a further amendment to the schedule to sustain long term control by providing high antibody levels into the age groups at which meningococcal carriage becomes more common. An adolescent booster dose at age 13-14 years was added to the schedule.

At the same time, JCVI considered a study that showed a single dose of some varieties of MenC vaccines at three months of age would be sufficient to prime infants against meningococcal serogroup C disease, and provide protection for the first year of life (Findlow *et al.*, 2011). Therefore the second dose at 4 months of age was removed from the routine schedule in 2013.

Serogroup B strains now account for over 80% of laboratory-confirmed cases submitted to the Health Protection Agency (HPA) Meningococcal Reference Unit and Scottish *Haemophilus*, *Legionella*, *Meningococcus* and *Pneumococcus* Reference Laboratory (SHLMPRL).

<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZMeningococcalDisease/>

### The meningococcal vaccination

Four variations of vaccine are available against meningococcal disease, three are conjugate vaccines and one plain polysaccharide vaccine:

- meningococcal serogroup C conjugate vaccine (MenC conjugate),
- *Haemophilus influenzae* type b / meningococcal serogroup C conjugate vaccine (Hib/MenC),
- quadrivalent meningococcal serogroup A, C, W and Y conjugate vaccine (MenACWY conjugate).
- quadrivalent meningococcal serogroup A, C, W and Y polysaccharide vaccine (MenACWY polysaccharide).

There are three licensed MenC conjugate vaccines available in the UK, Neisvac-C<sup>®</sup>, Menjugate Kit<sup>®</sup> and Meningitec<sup>®</sup>, and two ACWY conjugate vaccines, Menveo<sup>®</sup> and Nimenrix<sup>®</sup>. The only licensed Hib/MenC vaccine available in the UK is Menitorix<sup>®</sup>, and the only licensed MenACWY polysaccharide vaccine available in the UK is ACWY Vax.

### MenC conjugate vaccines

The MenC conjugate vaccines are made from capsular polysaccharide that has been extracted from cultures of serogroup C *Neisseria meningitidis*. The polysaccharide is linked (conjugated) to a carrier protein, according to the manufacturer's method. In the UK, MenC vaccines have been used that have been conjugated with either CRM197 (a non-toxic variant of diphtheria toxin) or tetanus toxoid. The conjugation increases the immunogenicity, especially in young children in whom the plain polysaccharide vaccines are less immunogenic. MenC vaccine confers no protection against other serogroups of meningococcal disease, such as serogroups A, B, W or Y.

### Hib/MenC conjugate vaccine

The Hib/MenC conjugate vaccine is made from capsular polysaccharides of *Haemophilus influenzae* type b and *Neisseria meningitidis* serogroup C, which are both conjugated to tetanus toxoid. The vaccine has been shown to elicit booster responses to both Hib and MenC when given in the second year of life to children who were primed in infancy with Hib and MenC conjugate vaccines.

### Quadrivalent (ACWY) conjugate vaccines

The MenACWY conjugate vaccines are made from capsular polysaccharide that have been extracted from cultures of serogroup A, C, W and Y *Neisseria meningitidis*. The polysaccharides are conjugated to a carrier protein. In the UK, MenACWY vaccines are conjugated with either CRM197 (a non-toxic variant of diphtheria toxin) or tetanus toxoid. The process of conjugation improves the immunogenicity, especially in young children and older people.

Although neither of the available vaccines is licensed for use in infants, data show a good antibody response to all serogroups after two doses of Menveo<sup>®</sup> conjugate vaccine (Snape *et al.*, 2008; Perrett *et al.*, 2009). The responses are better than seen with the polysaccharide vaccine (Borrow, 2009) and the response to serogroup C is comparable with that seen with the monovalent MenC conjugate vaccine (Southern *et al.*, 2009). Based on this and the experience with other conjugate vaccines, immunity is expected to be higher, longer-lasting and confer less risk of immunological tolerance than with the

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polysaccharide vaccine. For this reason, both conjugate vaccines are recommended in preference to polysaccharide vaccine in children from one to under five years of age. Menveo<sup>®</sup> is recommended for use in children below one year of age as there are some data on the use of Menveo<sup>®</sup> in that age group.

### Quadrivalent (ACWY) polysaccharide vaccine

The (non-conjugated) polysaccharide vaccine is made from the polysaccharide in the capsules of serogroups A, C, W and Y *Neisseria meningitidis* organisms. Young infants make some response to serogroup A, Y and W polysaccharides from three months of age (Peltola *et al.*, 1985; Cadoz *et al.*, 1985; Al-Mazrou *et al.*, 2005). However, protection is not long-lasting as immunological memory is not induced. Vaccine-induced immunity lasts approximately three to five years in older children and adults; in younger children, a more rapid decline in antibody has been noted (Frasch, 1995). In addition, polysaccharide vaccine may induce immune hyporesponsiveness when immune responses to second and subsequent doses of the same vaccine are attenuated (Jokhdar *et al.*, 2004; Khalil *et al.*, 2005). The response is strictly serogroup-specific and confers no protection against serogroup B organisms.

The above vaccines are inactivated, do not contain live organisms and cannot cause the diseases against which they protect.

**A vaccine against serogroup B organisms has been licensed for use in the UK, although the vaccine is not yet available on the UK market. No decision has yet been made regarding its introduction into the routine childhood immunisation schedule.**

### Storage

Vaccines should be stored in the original packaging at +2°C to +8°C and protected from light. All vaccines are sensitive to some extent to heat and cold. Heat speeds up the decline in potency of most vaccines, thus reducing their shelf life. Effectiveness of vaccines may be impaired if not stored at the correct temperature. Freezing may cause increased reactogenicity and loss of potency for some vaccines. It can also cause hairline cracks in the container, leading to contamination of the contents. For further information on storage see Chapter 3.

## Presentation

### MenC conjugate

The MenC conjugate vaccine is available either as a lyophilised powder for reconstitution with a diluent or as a suspension in a syringe. After reconstitution of the lyophilised suspension, the vaccine must be used within one hour.

Discard any vaccine that is unused one hour following reconstitution. Note: the diluent must not be frozen.

### Hib/MenC conjugate

Hib/MenC is supplied as a vial of white powder and 0.5ml of solvent in a pre-filled syringe. The vaccine must be reconstituted by adding the entire contents of the pre-filled syringe to the vial containing the powder. After addition of the solvent, the mixture should be shaken well until the powder is completely dissolved. After reconstitution, the vaccine should be administered promptly or allowed to stand between +2° and +8° and be used within 24 hours.

### Quadrivalent (ACWY) polysaccharide vaccine

The quadrivalent A, C, W and Y polysaccharide vaccine should be reconstituted immediately before use with the diluent supplied by the manufacturer. After reconstitution, the vaccine must be used within one hour. Discard any vaccine that is unused one hour following reconstitution. Note: the diluent must not be frozen.

### Quadrivalent (ACWY) conjugate vaccine

The quadrivalent conjugate ACWY vaccines are supplied as a powder in a vial, and 0.5ml solution in a pre-filled syringe. The vaccines must be reconstituted by adding the entire contents of the pre-filled syringe (containing MenCWY) to the vial containing the powder (containing MenA). After reconstitution, all the vaccine should be drawn up into the syringe and used immediately, but Menveo<sup>®</sup> may be held at or below 25°C for up to eight hours, and chemical and physical in-use stability has been demonstrated for 24 hours at 30°C for Nimenrix<sup>®</sup>.

## Dosage and schedule

### Routine MenC schedule

See Tables 22.1 and 22.2 in the 'Recommendations for the routine use of the MenC conjugate vaccines' section below.

### MenACWY conjugate schedule (see chapter 7)

See Table 22.3 in the 'Children and adults with asplenia, splenic dysfunction or complement deficiency' section below.

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### Quadrivalent (ACWY) quadrivalent polysaccharide vaccine

This vaccine is not included in the routine schedule, and should only be offered as a travel vaccination. Men ACWY quadrivalent conjugate vaccine is preferred to the polysaccharide vaccine in all instances.

Children over five years of age and adults:

- single dose of 0.5ml.

Reinforcing doses should be given at recommended intervals (see below).

### Administration

All meningococcal-containing vaccines are given intramuscularly into the upper arm or anterolateral thigh. This is to reduce the risk of localised reactions, which are more common when the vaccine is given subcutaneously (Mark *et al.*, 1999; Zuckerman, 2000; Diggle *et al.*, 2000). However, for individuals with a bleeding disorder, vaccines should be given by deep subcutaneous injection to reduce the risk of bleeding.

Meningococcal vaccines can be given at the same time as other vaccines such as pneumococcal, measles, mumps and rubella (MMR), diphtheria, tetanus, pertussis, polio and Hib. The vaccines should be given at a separate site, preferably in a separate limb. If given in the same limb, they should be given at least 2.5cm apart (American Academy of Pediatrics, 2006). The site at which each vaccine is given should be noted in the child's clinical record.

### Disposal

Equipment used for vaccination, including used vials, ampoules, or partially discharged vaccines should be disposed of at the end of a session by sealing in a proper, puncture-resistant 'sharps' box according to local authority regulations and guidance in the technical memorandum 07-01 (Department of Health, 2006).

### Recommendations for the routine use of the MenC conjugate vaccines

The objective of the routine immunisation programme is to protect those under 25 years of age and individuals outside this age range who may be at increased risk from meningococcal C disease.

### Immunisation schedule

The routine immunisation schedule, as revised in 2013, is set out in Table 22.1.

Table 22.1 Meningococcal C routine vaccination schedule

Age	Primary/Booster	Dose
Three months	Primary‡	One dose - Men C vaccine* (Neisvac C or Menjugate Kit only)
12-13 months	Booster	One dose - Hib/MenC vaccine*
Around 14 years	Booster	One dose - Men C vaccine*

‡ Although the summary of product characteristics for available MenC conjugate vaccines states that two doses should be given at least two months apart in those less than one year of age, evidence from a UK study shows that immunogenicity is adequate following a primary course of a single dose in infants (Findlow *et al.*, 2012).

\* If no doses of MenC vaccine have been received follow the 'Individuals with unknown or incomplete vaccination histories' table (Table 22.2)

Meningitec<sup>®</sup> vaccine does not provide adequate protection against meningococcal serogroup C disease when administered as single dose in infancy, and is therefore no longer recommended for use in those less than 12 months of age. Should Meningitec<sup>®</sup> have been given as part of the infant schedule (for example inadvertently or overseas), a second dose of Men C vaccine (preferably one containing a CRM conjugate such as Meningitec<sup>®</sup> or Menjugate Kit<sup>®</sup>) should be given at least one month after the first dose.

### Individuals with unknown or incomplete vaccination histories

When a child born in the UK presents with an inadequate immunisation history, every effort should be made to clarify what immunisations they may have had (see Chapter 11). Children coming to the UK who have a history of immunisation in their country of origin may not have been offered protection with all the antigens currently used in the UK, and they may not have received MenC-containing vaccines.

[http://www.who.int/immunization\\_monitoring/en/globalsummary/schedule\\_select.cfm](http://www.who.int/immunization_monitoring/en/globalsummary/schedule_select.cfm)

Children coming from developing countries, from areas of conflict, or from hard-to-reach population groups may not have been fully immunised. Where there is no reliable history of previous immunisation, it should be assumed that they are unimmunised and the full UK recommendations should be followed (see Chapter 11). Table 22.2 sets out the schedule for those with unknown or incomplete vaccination histories.

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Table 22.2 Meningococcal C vaccination schedule for those with unknown or incomplete vaccination histories

Age	Dose
< One year	Give one dose of Men C vaccine (Neisvac C or Menjugate Kit) and follow schedule from 12-13 months (leaving at least one month between primary and booster doses)
≥ One year to less than 10 years	Give one dose of Men C (or Hib/MenC if unvaccinated for Hib)
Ten years to less than 25 years	<ul style="list-style-type: none"><li>● If has never received vaccine give one dose of MenC – no further vaccination is then required</li><li>● If received MenC since reaching 10 years of age no further vaccination is required</li><li>● If last received MenC vaccine under ten years of age, give MenC with teenage booster (at around 14 years of age)</li></ul>

Children over the age of one and under the age of ten years who have not received any MenC vaccine should be offered a single dose of MenC or Hib/MenC (if they are also unvaccinated for Hib). The response at this age is very good even where no infant doses have been received. These children should still receive the teenage booster when they reach the target age.

Children who reach the target age for the teenage booster who were vaccinated according to the previous vaccine schedules (without a toddler booster) should be offered a single dose. Children above the age of ten years who have not received any MenC may receive the teenage booster early (See Table 22.2).

### Children and adults with asplenia, splenic dysfunction or complement deficiency

Children and adults with asplenia or splenic dysfunction may be at increased risk of invasive meningococcal infection. Such individuals, irrespective of age or interval from splenectomy, may have a sub-optimal response to the vaccine (Balmer *et al.*, 2004). Children and adults with complement deficiency (Figueroa *et al.*, 1991), or on Eculizumab therapy, may be at increased risk of invasive meningococcal infection.

Given the increased risk, additional vaccinations against meningococcal disease are advised for individuals with asplenia or splenic dysfunction or when complement deficiency is diagnosed depending on age and vaccination history.

Table 22.3 Meningococcal ACWY vaccination schedule for children and adults with asplenia, splenic dysfunction or complement deficiency.

Age	Dose
< One year	Vaccinate according to the routine schedule, Give one dose of MenACWY conjugate at least one month after the Hib/MenC booster dose
≥ One years	One dose of Hib/MenC, and one dose of MenACWY conjugate at least one month apart.

All individuals who are to receive Eculizumab therapy, should be vaccinated at least two weeks prior to commencement of therapy (Soliris<sup>®</sup> SPC). For the full list of immunisations for these groups, see Table 7.1 in chapter 7. This advice applies to all newly diagnosed patients. Where an opportunity arises, and depending on individual patient's circumstances, MenACWY conjugate vaccination could be considered for those that only received protection against meningococcal C from earlier vaccinations.

## Reinforcing immunisation for children and adults with asplenia, splenic dysfunction or complement deficiency

### Meningococcal ACWY conjugate vaccine.

Children who have not previously received Meningococcal ACWY conjugate vaccine above the age of one should be given a dose of Meningococcal ACWY conjugate vaccine if they are travelling to an area that puts them at risk from meningococcal infection. The meningococcal ACWY conjugate vaccine is likely to provide better protection than the polysaccharide vaccine. However, the need for, and the timing of, a booster dose of Meningococcal ACWY conjugate vaccine has not yet been determined.

### Meningococcal ACWY polysaccharide vaccine.

Men ACWY quadrivalent conjugate vaccine is preferred to the polysaccharide vaccine in all instances. Those who had received polysaccharide vaccines in the past should be vaccinated with conjugate vaccine as above.

## Individuals who are travelling or going to reside abroad

All travellers should undergo a careful risk assessment that takes into account their itinerary, duration of stay and planned activities. In some areas of the world, the risk of acquiring meningococcal infection, particularly of developing serogroup A disease, is much higher than in the UK. Individuals who are particularly at risk are visitors who live or travel 'rough', such as backpackers, and those living or working with local people. Large epidemics of both

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serogroup A and W meningococcal infection have occurred in association with Hajj pilgrimages, and proof of vaccination against A, C, W and Y serogroups is now a visa entry requirement for pilgrims and seasonal workers travelling to Saudi Arabia.

Epidemics, mainly of serogroup A and more recently serogroup W infections, occur unpredictably throughout tropical Africa but particularly in the savannah during the dry season (December to June). Immunisation is recommended for long-stay or high-risk visitors to sub-Saharan Africa, for example, those who will be living or working closely with local people, or those who are backpacking.

From time to time, outbreaks of meningococcal infection may be reported from other parts of the world, including the Indian sub-continent and other parts of Asia [www.hpa.org.uk/cdr/archives/2005/cdr1905.pdf](http://www.hpa.org.uk/cdr/archives/2005/cdr1905.pdf)

[http://www.who.int/csr/don/2005\\_01\\_28a/en/index.html](http://www.who.int/csr/don/2005_01_28a/en/index.html)

Where such outbreaks are shown to be due to vaccine-preventable serogroups, vaccination may be recommended for certain travellers to the affected areas.

Country-specific recommendations and information on the global epidemiology of meningococcal disease can be found on the following websites:

[www.nathnac.org](http://www.nathnac.org)

[www.travax.nhs.uk](http://www.travax.nhs.uk).

Note: MenC conjugate vaccine protects against serogroup C disease only. Individuals travelling abroad (see above) should be immunised with an appropriate quadrivalent (ACWY) vaccine, even if they have previously received the MenC conjugate vaccine.

### Recommendations for the use of the quadrivalent (ACWY) vaccines for travel

Both polysaccharide ACWY (ACWY Vax) and conjugate ACWY vaccines are available. In children under five years old, it is recommended that ACWY conjugate vaccine be used in preference to ACWY Vax because of the better immune response and to reduce the risk of hyporesponsiveness (Jokhdar *et al.*, 2004; Khalil *et al.*, 2005). In children aged over five years and adults, ACWY conjugate vaccine should be used in preference to the polysaccharide vaccine to reduce the risk of hyporesponsiveness and to provide better protection. – see Table 22.4 below.

Table 22.4 Recommendations for the use of quadrivalent meningococcal ACWY vaccines for travel

Recommendations on immunisation procedures are based on currently available evidence and experience of best practice. In some circumstances, this advice may differ from that in vaccine manufacturers' Summaries of Product Characteristics (SPCs). When this occurs, the recommendations in this book (which are based on current expert advice received from the Joint Committee on Vaccination and Immunisation (JCVI)) should be followed (see Chapter 4).

Age	Quadrivalent vaccine	
	Conjugate MenACWY	Polysaccharide MenACWY (ACWY Vax)
Infants under one year*	Menveo® <ul style="list-style-type: none"> <li>● First dose of 0.5ml</li> <li>● Second dose of 0.5ml one month after the first dose.</li> </ul>	<ul style="list-style-type: none"> <li>● Not recommended</li> </ul>
Children aged one year to four years	Menveo® or Nimenrix® <ul style="list-style-type: none"> <li>● Single dose of 0.5ml.</li> </ul>	<ul style="list-style-type: none"> <li>● Not recommended</li> </ul>
Children aged five years to ten years	Menveo® or Nimenrix® (either preferred to polysaccharide vaccine) <ul style="list-style-type: none"> <li>● Single dose of 0.5ml.</li> </ul>	<ul style="list-style-type: none"> <li>● Single dose of 0.5ml.</li> </ul>
Individuals aged 11 years and older	Menveo® or Nimenrix® (either preferred to polysaccharide vaccine) <ul style="list-style-type: none"> <li>● Single dose of 0.5ml.</li> </ul>	<ul style="list-style-type: none"> <li>● Single dose of 0.5ml.</li> </ul>

\* Replace the MenC vaccine with MenACWY conjugate vaccine if the infant requires MenACWY conjugate vaccine at the same time as the routine MenC vaccinations. If the infant has already had two MenC vaccinations then two MenACWY conjugate vaccines should also be given.

### Contraindications

There are very few individuals who cannot receive meningococcal vaccines. When there is doubt, appropriate advice should be sought from a consultant paediatrician, immunisation co-ordinator or consultant in communicable disease control, rather than withhold immunisation. The vaccines should not be given to those who have had:

- a confirmed anaphylactic reaction to a previous dose of the vaccine, or
- a confirmed anaphylactic reaction to any constituent or excipient of the vaccine.

### Precautions

Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation may be postponed until they have recovered fully. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

### Pregnancy and breast-feeding

Meningococcal vaccines may be given to pregnant women when clinically indicated. There is no evidence of risk from vaccinating pregnant women or those who are breast-feeding with inactivated virus or bacterial vaccines or toxoids (Granoff *et al.*, 2008). In cases where meningococcal immunisation has been inadvertently given in pregnancy, there has been no evidence of fetal problems.

### Premature infants

It is important that premature infants have their immunisations at the appropriate chronological age, according to the schedule. The occurrence of apnoea following vaccination is especially increased in infants who were born very prematurely.

Very premature infants (born  $\leq$  28 weeks of gestation) who are in hospital should have respiratory monitoring for 48-72 hrs when given their first immunisation, particularly those with a previous history of respiratory immaturity. If the child has apnoea, bradycardia or desaturations after the first immunisation, the second immunisation should also be given in hospital, with respiratory monitoring for 48-72 hrs (Ohlsson *et al.*, 2004; Pfister *et al.*, 2004; Schulzke *et al.*, 2005; Pourcyrous *et al.*, 2007; Klein *et al.*, 2008).

As the benefit of immunisation is high in this group of infants, immunisation should not be withheld or delayed.

## Immunosuppression and HIV infection

Individuals with immunosuppression and human immunodeficiency virus (HIV) infection (regardless of CD4 count) should be given meningococcal vaccines in accordance with the routine schedule. These individuals may not make a full antibody response. Re-immunisation should be considered after treatment is finished and recovery has occurred. Specialist advice may be required.

Further guidance is provided by the Royal College of Paediatrics and Child Health ([www.rcpch.ac.uk](http://www.rcpch.ac.uk)), the British HIV Association (BHIVA) *Immunisation guidelines for HIV-infected adults* (BHIVA, 2006) and the Children's HIV Association of UK and Ireland (CHIVA) immunisation guidelines ([www.bhiva.org/chiva](http://www.bhiva.org/chiva)).

## Adverse reactions

### MenC conjugate vaccine

Pain, tenderness, swelling or redness at the injection site and mild fevers are common in all age groups. In infants and toddlers, crying, irritability, drowsiness, impaired sleep, reduced eating, diarrhoea and vomiting are commonly seen. In older children and adults, headaches, myalgia and drowsiness may be seen.

Neurological reactions such as dizziness, febrile/afebrile seizures, faints, numbness and hypotonia following MenC conjugate vaccination are very rare.

### Hib/MenC conjugate

Mild side effects such as irritability, loss of appetite, pain, swelling or redness at the site of the injection and slightly raised temperature commonly occur. Less commonly crying, diarrhoea, vomiting, atopic dermatitis, malaise and fever over 39.5°C have been reported.

### Quadrivalent (ACWY) conjugate vaccine

For Menveo<sup>®</sup>, very common or common reported reactions included injection site reactions including pain, erythema, induration and pruritus. Other very common or common reactions include headache, nausea, rash and malaise. Reports of all adverse reactions can be found in the Summary of Product Characteristics for Menveo<sup>®</sup> (Novartis, 2010).

## Meningococcal

For Nimenrix<sup>®</sup>, very common or common reported reactions included injection site reactions including pain, erythema, and swelling. Other very common or common reactions include irritability, drowsiness, headache, nausea, and loss of appetite. Reports of all adverse reactions can be found in the Summary of Product Characteristics for Nimenrix<sup>®</sup> (GSK, 2012).

### Quadrivalent (ACWY) polysaccharide vaccine

Generalised reactions are rare, although pyrexia occurs more frequently in young children than in adults.

Injection site reactions occur in approximately 10% of recipients and last for approximately 24 to 48 hours.

#### Reporting adverse events

Anyone can report a suspected adverse reaction to the Medical and Healthcare products Regulatory Agency (MHRA) using the Yellow Card reporting scheme ([www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)).

All suspected adverse reactions to vaccines occurring in children or in individuals of any age after vaccination with vaccines labelled with a black triangle (▼), should be reported to the Commission on Human Medicines using the Yellow Card scheme. Serious suspected adverse reactions to vaccines in adults should be reported through the Yellow Card scheme.

### Management of suspected cases, contacts and outbreaks

Current recommendations from NICE are that children and young people with suspected bacterial meningitis without non-blanching rash should be transferred directly to secondary care without giving parenteral antibiotics. If urgent transfer to hospital is not possible (for example, in remote locations or because of adverse weather conditions), antibiotics should be administered to children and young people with suspected bacterial meningitis.

For suspected meningococcal disease (meningitis with non-blanching rash or meningococcal septicaemia) parenteral antibiotics (intramuscular or intravenous benzylpenicillin) should be given at the earliest opportunity, either in primary or secondary care, but urgent transfer to hospital should not be delayed in order to give the parenteral antibiotics.

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

[http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb\\_C/1195733822509](http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733822509)

## Management of contacts

For public health management of contacts of cases and outbreaks, advice must be sought from the local health protection unit. Household contacts of cases of meningococcal infection are at increased risk of developing the disease. This risk is highest in the first seven days following onset in the index case but persists for at least four weeks. Immediate risk can be reduced by the administration of antibiotic prophylaxis to the whole contact group.

For prophylaxis, the use of single dose ciprofloxacin is now recommended in preference to rifampicin, particularly because it is a single dose and is readily available in high street pharmacies. Ciprofloxacin as a single dose of 500mg may be given for adults (250mg for children aged five to 12 years and 125mg for those aged one month to four years). Alternative options are discussed at [www.hpa.org.uk/webc/HPAwebFile/HPAweb\\_C/1194947389261](http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947389261)

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

For confirmed serogroup A, W or Y infections, vaccination with a quadrivalent conjugate vaccine should be offered to all close contacts of any age (two doses one month apart if aged under one year; one dose in older individuals).

MenC conjugate vaccine should also be offered according to the recommended national schedule to any unimmunised index cases under the age of 25 years (whatever the serogroup). Although recurrent serogroup C disease is rare, this policy ensures that persons in this age group are given equivalent protection to their age-matched immunised peers.

Chemoprophylaxis should be given as soon as possible, while the decision to offer vaccine should be made when the results of serogrouping are available.

**Any case provides an opportunity to check the MenC vaccine status of the index case and contacts, and to ensure that individuals under the age of 25 years have been fully immunised according to the UK schedule. Current vaccines do not protect against serogroup B meningococcal infection.**

### Management of local outbreaks

In addition to sporadic cases, outbreaks of meningococcal infections can occur particularly in closed or semi-closed communities such as schools, military establishments and universities. Advice on the management of such outbreaks should be obtained from the local or regional health protection unit. Advice on the use of meningococcal vaccines in outbreaks is available from: Public Health England, Colindale (Tel: 020 8200 6868) Health Protection Agency, Meningococcal Reference Unit (Tel: 0161 276 5698) Health Protection Scotland (Tel: 0141 300 1100) Scottish *Haemophilus*, *Legionella*, *Meningococcus* and *Pneumococcus* Reference Laboratory (Tel: 0141 201 3836).

### Supplies

Some or all of the following Meningitis C conjugate vaccines will be available at any one time:

- Menjugate<sup>®</sup> – manufactured by Novartis Vaccines
- NeisVac-C<sup>®</sup> – manufactured by Baxter Healthcare
- Menitorix<sup>®</sup> (Hib/MenC) – manufactured by GlaxoSmithKline
- Meningitec<sup>®</sup> – manufactured by Pfizer (not suitable for the single infant dose).

In England, these vaccines should be ordered online only via the ImmForm website ([www.immform.dh.gov.uk](http://www.immform.dh.gov.uk)) and are distributed by Movianto UK (Tel: 01234 248631) as part of the national childhood immunisation programme.

Centrally purchased vaccines for the national immunisation programme for the NHS can only be ordered via ImmForm. Vaccines for use for the national childhood immunisation programme are provided free of charge. Vaccines for private prescriptions, occupational health use or travel are NOT provided free of charge and should be ordered from the manufacturers. Further information about ImmForm is available at <http://immunisation.dh.gov.uk/immform-helplets/> or from the ImmForm helpdesk at [helpdesk@immform.org.uk](mailto:helpdesk@immform.org.uk) or Tel: 0844 376 0040.

In Northern Ireland, supplies should be obtained under the normal childhood vaccines distribution arrangements, details of which are available by contacting the Regional Pharmaceutical Procurement Service on 028 9442 4346.

In Scotland, supplies should be obtained from the local childhood vaccine holding centres. Details of these are available from Scottish Healthcare Supplies (Tel: 0141 282 2240).

Quadrivalent ACWY vaccines are not part of the national childhood immunisation programme and should be ordered directly from manufacturers:

- ACWY Vax (Quadrivalent ACWY polysaccharide vaccine) – manufactured by GlaxoSmithKline (Tel: 0808 100 9997).
- Menveo® (Quadrivalent conjugate ACWY vaccine) – manufactured by Novartis® (Tel: 08457 451500).
- Nimenrix® (Quadrivalent conjugate ACWY vaccine) – Manufactured by GlaxoSmithKline® (Tel: 0800 221 441)
- Quadrivalent (ACWY) conjugate vaccine for use in contacts of cases of outbreaks serogroup A, W or Y infections, may be accessed through:

[https://www.wp.dh.gov.uk/immunisation/files/2011/11/ImmFormHelpsheet-13\\_v3acc.pdf](https://www.wp.dh.gov.uk/immunisation/files/2011/11/ImmFormHelpsheet-13_v3acc.pdf)

For further information about vaccines available via ImmForm, please see ImmForm Helpsheet 13

Public Health England, Centre for Infections (Tel: 020 8200 6868)

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