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. There are at least 13 serogroups, of which groups B, C and Y were historically the most common in the UK. Other less common serogroups included A, W135, 29E and Z. The 13 serogroups can be further subdivided by serotyping and serosubtyping and by sulphonamide sensitivity. Increasing use of molecular-based methods allows further classification of the organisms and identification of specific clonal complexes that appear to be associated with invasive disease.

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 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 a coma.

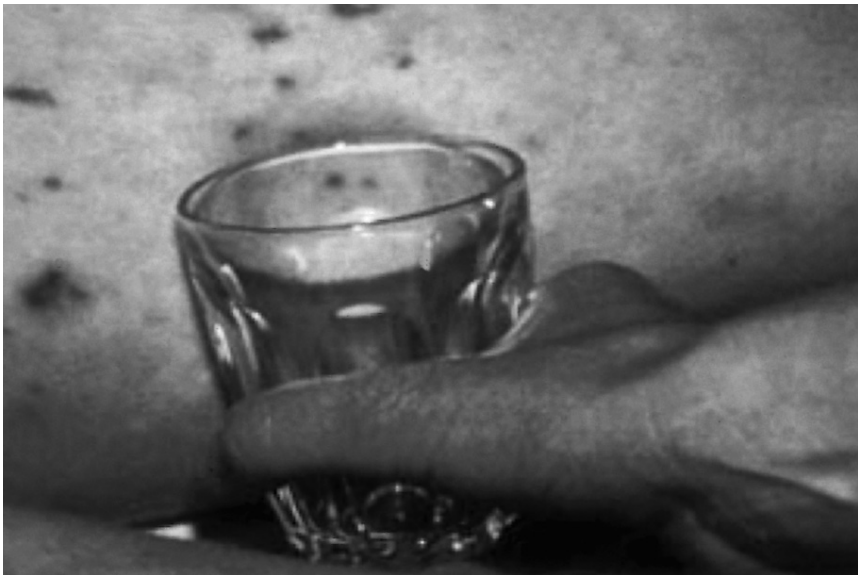

Figure 22.1 The 'glass' test (*picture courtesy of Meningitis Research Foundation)*

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 (Cartwright, 1995). It is not fully understood why the 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.

The incidence of meningococcal disease is highest in infants under one year of age, followed by children aged one to five years. The next highest incidence is seen in young people aged 15 to 19 years.

Overall mortality remains around 10% in the UK (Ramsay *et al.*, 1997; Goldacre *et al.*, 2003). Mortality is higher in cases with septicaemia than in those with meningitis alone (Davison *et al.*, 2002). Case fatality ratios

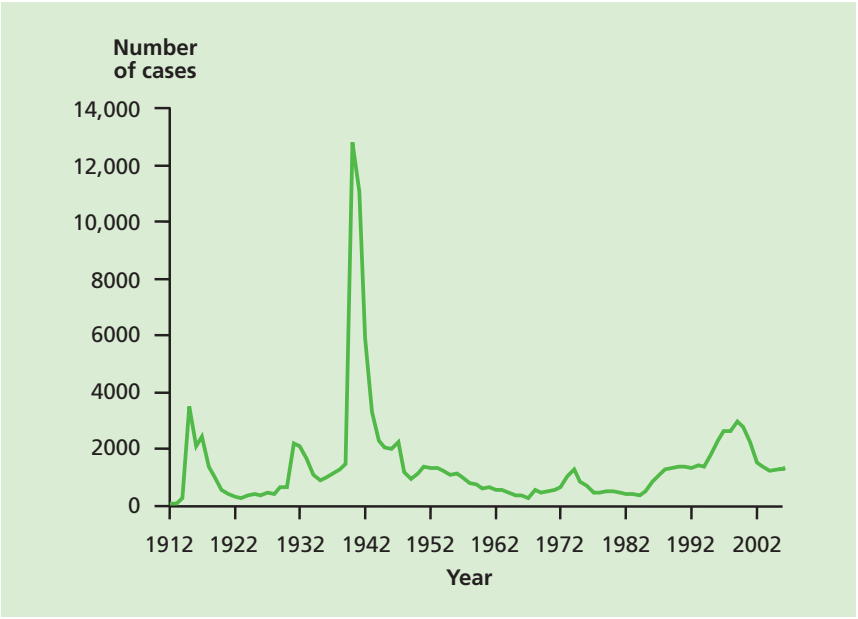

Figure 22.2 Notifications of meningococcal disease, England and Wales 1912–2004

increase with age and were higher in individuals with serogroup C than with 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

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 serogroup W135 and X.

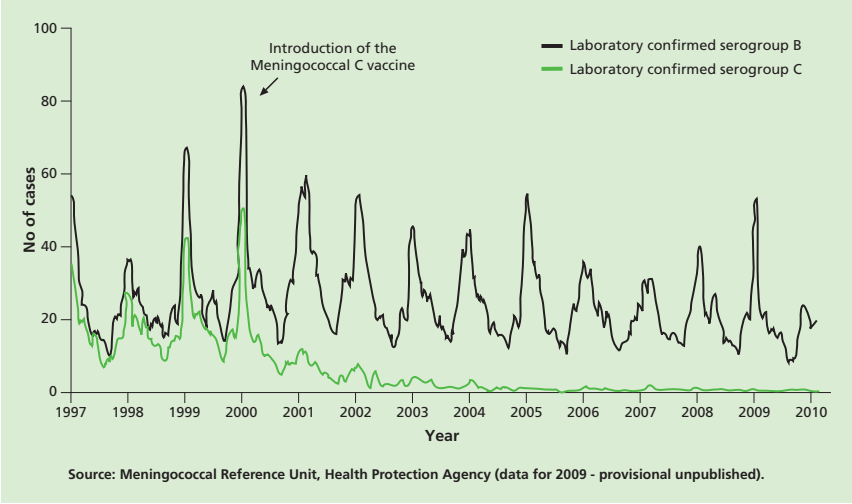

Figure 22.3 Laboratory-confirmed cases of meningococcal disease, England and Wales, five weekly moving averages. 1997 to 2009.

There have been large epidemics of meningococcal disease 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, there was an increase in W135 infections at the Hajj which resulted in a number of cases in UK pilgrims and their families (Hahne *et al*., 2002). Evidence of receipt of quadrivalent vaccine (serogroups A, C, Y, W135) became an entry requirement in 2002. Following this recommendation, W135 cases have returned to very low levels in the UK.

In the UK, large epidemics of meningococcal disease 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.

Vaccines based on the serogroup C polysaccharide 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 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. All children and adolescents under the age of 18 years were immunised over a two-year period. In January 2002, the campaign was extended to include all 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) (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 therefore reduced risk of exposure (Trotter *et al.*, 2003). This phenomenon, known as indirect protection or herd immunity, has contributed to the number of cases falling to an all time low of only ten in 2009.

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 as Hib/MenC) was introduced at 12 months of age.

Serogroup B strains now account for around 90% of laboratory-confirmed cases submitted to the Health Protection Agency (HPA) Meningococcal Reference Unit (Health Protection Agency) http://www.hpa.org.uk/cdph/issues/CDPHVol15/ no3/Meningococcal_ Guidelines.pdf

The meningococcal vaccination

MenC conjugate vaccine

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, W135, or Y.

Hib/MenC conjugate vaccine

The Hib/MenC conjugate vaccine is made from capsular polysaccharides of *Haemophilus influenzae* type b and *Neisseria meningitidis* group 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) polysaccharide vaccine

The plain (non-conjugated) polysaccharide vaccine is made from the polysaccharide in the capsules of serogroups A, C, W135 and Y *Neisseria meningitidis* organisms. Young infants make some response to serogroup A, Y and W135 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.

Quadrivalent (ACWY) conjugate vaccine

The MenACWY conjugate vaccine (Menveo®) is made from capsular polysaccharide that has been extracted from cultures of serogroup A, C, W135 and Y *Neisseria meningitidis.* The polysaccharides are conjugated to CRM197. The process of conjugation improves the immunogenicity, especially in young children and older people.

Although the vaccine is not yet licensed for infants, data show a better antibody response to all serogroups after two doses of conjugate vaccine (Snape *et al.*, 2008; Perrett *et al.*, 2009) than seen with the plain polysaccharide vaccine (Borrow, 2009); the response to serogroup C is comparable with that seen with the monovalent MenC conjugate vaccine (Southern *et al.*, 2008). 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 the plain vaccine. For this reason, conjugate vaccine is recommended in preference to plain vaccine in children under five years of age.

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

At present, no available vaccine is effective against serogroup B organisms.

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 cannot be guaranteed for vaccines unless they have been 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.

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 well shaken 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 (ACW135Y) polysaccharide vaccine

The quadrivalent A, C, W135 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 (ACW135Y) conjugate vaccine

The quadrivalent conjugate ACWY vaccine (Menveo®) is supplied as a powder in a vial, and 0.5ml solution in a pre-filled syringe. The vaccine 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 may be held at or below 25°C for up to eight hours.

Dosage and schedule

MenC vaccine

Infants under one year of age:

- First dose of 0.5ml of MenC vaccine.
- Second dose of 0.5ml, one month after the first dose.
- A third dose of 0.5ml of MenC-containing vaccine should be given at the recommended interval (see below).

Children over one year of age, adults under 25 years and individuals outside this age range who may be at increased risk from meningococcal C disease should have a single dose of MenC-containing vaccine.

Combined Hib/MenC

Children over one and under two years of age:

- One dose of 0.5ml.

Quadrivalent (ACWY) conjugate vaccine

Children over two months of age and under one year:

- First dose of 0.5ml.
- Second dose of 0.5ml at least one month after the first dose.

A reinforcing dose of 0.5ml should be given 12 months after the primary course if the child continues to be at risk.

Children aged over one year of age and adults:

- Single dose of 0.5ml.

The need for, and timing of, a reinforcing dose has not yet been determined (see below).

Quadrivalent (ACWY) polysaccharide vaccine

Children over five years of age and adults:

- Single dose of 0.5ml.

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

Administration

The 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 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 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.

Primary immunisation

Infants under one year of age

The primary course of MenC vaccination consists of two doses, with an interval of one month between each dose. The recommended age for vaccination is at three and four months of age. If the primary course is interrupted it should be resumed but not repeated (see below). The currently available MenC vaccines are now licensed for use in a two-dose schedule from two months of age. Although the licence states that two doses should be given at least two months apart, evidence from UK studies shows that immunogenicity is adequate in children immunised at a one-month interval (Southern *et al*., 2006).

Children from one year of age and adults

The primary course of MenC vaccine for this age group is one dose. If the primary course in children under one year was not completed, then a single booster dose of Hib/MenC vaccine should be given, at least one month after the last dose.

All individuals under 25 years and other individuals at elevated risk, regardless of their age, should be immunised with a single dose of a MenC-containing vaccine. Any unvaccinated individual attending university, irrespective of age, should be immunised before they enrol or as soon as possible thereafter.

Reinforcing immunisation

A reinforcing (booster) dose of Hib/MenC is recommended at 12 months of age for children who have received a complete primary course of two doses of MenC vaccine. The Hib/MenC vaccine can be given at the same time as the pneumococcal conjugate and MMR vaccines.

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 in their country of origin (http://www.who.int/immunization_monitoring/en/globalsummary/scheduleselect.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).

A child who has not completed the primary course (and is under one year of age) should have the outstanding doses at appropriate intervals (see above). If an individual is coming into the UK to attend university and has not previously been immunised against group C disease (with either polysaccharide or conjugate vaccine), they should receive one dose of a MenC containing vaccine as soon as possible.

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 may be at increased risk of invasive meningococcal infection (Figueroa *et al.*, 1991).

Given the increased risk, additional vaccinations against meningococcal disease are advised for individuals who develop asplenia or splenic dysfunction or when complement deficiency is diagnosed depending on age and vaccination history. 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 circumstances, an additional MenACWY conjugate vaccination could be considered for patients that only received protection against meningococcal C from earlier vaccinations.

Children under two years of age

These individuals should be vaccinated according to the UK routine childhood schedule, which includes a booster of Hib/MenC and PCV given at 12 months of age. A dose of MenACWY conjugate vaccine should be given at least one month after the Hib/MenC and PCV boosters.

After the second birthday, an additional dose of Hib/MenC should be given. If the individual received their routine pneumococcal booster dose as PCV7 (before April 2010) an additional dose of PCV13 should be offered at the same time, followed by a dose of PPV two months later. If the child was routinely boosted with PCV13 (after April 2010) a dose of PPV should be given with the Hib/MenC booster.

Fully vaccinated individuals over two and under five years of age

These individuals should receive one additional dose of Hib/MenC and PCV13 (as they will have received PCV7). One month after this, they should receive a dose of MenACWY conjugate vaccine. PPV should be given at least two months after the last dose of PCV13.

Previously unvaccinated individuals over two and under five years of age

These individuals should receive one dose of Hib/MenC vaccine with a dose of PCV13. One month after this, a dose of MenACWY conjugate vaccine should be given, followed by PCV13 one month later. Two months after the last dose of PCV13, PPV should be given.

Individuals over five years of age regardless of vaccination status

These individuals should receive one dose of Hib/MenC vaccine with a dose of PPV. One month after this, a dose of MenACWY conjugate vaccine should be given.

Reinforcing immunisation

Meningococcal ACWY conjugate vaccine (Menveo®)

Children over one year of age who have previously received one, two or three doses of Menveo® as infants should be given an additional dose of Menveo® if they are travelling to an area that puts them at risk from meningococcal infection.

The meningococcal ACWY conjugate vaccine is likely to provide longer lasting protection than the polysaccharide vaccine. However, the need for, and the timing of, a booster dose of Menveo® has not yet been determined.

Meningococcal ACWY polysaccharide vaccine

A reinforcing dose should be given every five years to those at continued risk. Children who were under five years when they were first vaccinated should be given a booster dose after 2–3 years if they remain at high risk.

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 serogroup A and W135 meningococcal infection have occurred in association with Hajj pilgrimages, and proof of vaccination against A, C, W135 and Y serogroups is now a visa entry requirement for pilgrims and seasonal workers travelling to Saudi Arabia.

Epidemics, mainly group A and more recently W135 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 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 and 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 (Menveo®) vaccines are available. In children, under five years old, it is recommended that Menveo® should be used off-label 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, Menveo® should be given to provide better and longer lasting protection.

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).

	Quadrivalent vaccine	
Age	**Conjugate MenACWY (Menveo®)**	**Polysaccharide MenACWY (ACWY Vax)**
Infants under one year*	'off label' • First dose of 0.5ml. • Second dose of 0.5ml one month after the first dose.	Not recommended
Children aged one year to four years	'off label' • Single dose of 0.5ml.	Not recommended
Children aged five years to ten years	'off label' (but preferred) • Single dose of 0.5ml.	• Single dose of 0.5ml.
Individuals aged 11 years and older	(preferred) • Single dose of 0.5ml.	• Single dose of 0.5ml.

* 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
- a confirmed anaphylactic reaction to any constituent of the vaccine, including meningococcal polysaccharide, diphtheria toxoid or the CRM197 carrier protein or tetanus toxoid.

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 ≤ 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), 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).

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 (ACW135Y) conjugate vaccine

For Menveo®, 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® (Novartis, 2010).

Quadrivalent (ACW135Y) 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).

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.

(www.guidance.nice.org.uk/CG102/NICEGuidance/pdf/English)

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/Topics/InfectiousDiseases/InfectionsAZ/MeningococcalDisease/Guidelines/

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, W135 or Y infections, vaccination with a quadrivalent conjugate vaccine (Menveo®) 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: Health Protection Agency, Colindale (Tel: 020 8200 6868) Health Protection

Agency, Meningococcal Reference Unit (Tel: 0161 276 5698) Health Protection Scotland (Tel: 0141 300 1100) Scottish Meningococcal and Pneumococcal Reference Laboratory (Tel: 0141 201 3836).

Supplies

Meningitis C conjugate:

- Menjugate® – manufactured by Novartis Vaccines
- NeisVac-C® – manufactured by Baxter Healthcare
- Menitorix® (Hib/MenC) – manufactured by GlaxoSmithKline.

These vaccines are supplied by Movianto UK (Tel: 01234 248631) as part of the national childhood immunisation programme.

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

- ACWY Vax (Quadrivalent ACWY polysaccharide vaccine) – manufactured by GlaxoSmithKline (Tel: 0808 100 9997).
- Menveo® (Quadrivalent conjugate ACWY vaccine) – manufactured by Novartis® (Tel: 08457 451500).
- Quadrivalent (ACWY) conjugate vaccine (Menveo®) for use in contacts of cases of outbreaks serogroup A, W135 or Y infections, may be accessed through:

Health Protection Agency, Centre for Infections (Tel: 020 8200 6868)

References

Al-Mazrou Y, Khalil M, Borrow R *et al.* (2005) Serologic responses to ACYW135 polysaccharide meningococcal vaccine in Saudi children under 5 years of age. *Infect Immun* **73**(5): 2932-9.

American Academy of Pediatrics (2006) Active Immunization. In: Pickering LK (ed.) *Red Book: 2006. Report of the Committee on Infectious Diseases.* 27th edition. Elk Grove Village, IL: American Academy of Pediatrics , p 9-54.

Balmer P, Falconer M, McDonald P *et al.* (2004) Immune response to meningococcal serogroup C conjugate vaccine in asplenic individuals. *Infect Immun* **72**(1): 332-7.

Booy R, Habibi P, Nadel S *et al.* (2001) Reduction in case fatality rate from meningococcal disease associated with improved healthcare delivery. *Arch Dis Child* **85**(5): 386-90.

Borrow R (2009) Meningococcal disease and prevention at the Hajj. *Travel Med Infect Dis* **7**(4): 219-25.

Cadoz M, Armand J, Arminjon F *et al.* (1985) Tetravalent (A, C, Y, W 135) meningococcal vaccine in children: immunogenicity and safety. *Vaccine* **3**(3): 340-2.

Cartwright K (1995) The Clinical Spectrum of Meningococcal Disease. In: Cartwright K (ed.) *Meningococcal disease*. Chichester, UK: John Wiley & Sons, pp 115-46.

Davison KL, Ramsay ME, Crowcroft NS *et al.* (2002) Estimating the burden of serogroup C meningococcal disease in England and Wales. *Commun Dis Public Health* **5**(3): 213-9.

Department of Health (2006) *Health Technical Memorandum 07-01: Safe Management of Healthcare Waste.* http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_063274. Accessed: July 2008.

Diggle L and Deeks J (2000) Effect of needle length on incidence of local reactions to routine immunisation in infants aged 4 months: randomised controlled trial. *BMJ* **321**(7266): 931-3.

Erickson L and De Wals P (1998) Complications and sequelae of meningococcal disease in Quebec, Canada, 1990-1994. *Clin Infect Dis* **26**(5): 1159-64 .

Figueroa JE and Densen P (1991) Infectious diseases associated with complement deficiencies. *Clin Microbiol Rev* **4**(3): 359-95.

Frasch CE (1995) Meningococcal Vaccines: Past, Present and Future. In: Cartwright K (ed.) *Meningococcal disease*. Chichester, UK: John Wiley & Sons, p 245-83.

Goldacre MJ, Roberts SE and Yeates D (2003) Case fatality rates for meningococcal disease in an English population, 1963-98: database study. *BMJ* **327**(7415): 596-7.

Granoff DM, Harrison LH and Borrow R (2008) Section 2: Licensed Vaccines - Meningococcal Vaccines. In: Plotkin S, Orenstein W and Offit P (ed.) *Vaccines*. 5th edition. Elsevier Inc., p 399-434.

Hahne S, Handford S and Ramsay M (2002) W135 meningococcal carriage in Hajj pilgrims. *Lancet* **360**(9350): 2089-90.

Jokhdar H, Borrow R, Sultan A *et al.* (2004) Immunologic hyporesponsiveness to serogroup C but not serogroup A following repeated meningococcal A/C polysaccharide vaccination in Saudi Arabia. *Clin Diagn Lab Immunol* **11**(1): 83-8.

Jones D (1995) Epidemiology of Meningococcal Disease in Europe and the USA. In: Cartwright K (ed.) *Meningococcal disease*. Chichester, UK: John Wiley & Sons, p 147-58.

Khalil M, Al-Mazrou Y, Balmer P *et al.* (2005) Immunogenicity of meningococcal ACYW135 polysaccharide vaccine in Saudi children 5 to 9 years of age. *Clin Diagn Lab Immunol* **12**(10): 1251-3.

Klein NP, Massolo ML, Greene J *et al.* (2008) Risk factors for developing apnea after immunization in the neonatal intensive care unit. *Pediatrics* **121**(3): 463-9.

Maiden MC and Stuart JM (2002) Carriage of serogroup C meningococci one year after meningococcal C conjugate polysaccharide vaccination. *Lancet* **359**(9320): 1829-31.

Mark A, Carlsson RM and Granstrom M (1999) Subcutaneous versus intramuscular injection for booster DT vaccination of adolescents. *Vaccine* **17**(15-16): 2067-72.

Miller E, Salisbury D and Ramsay M (2001) Planning, registration, and implementation of an immunisation campaign against meningococcal serogroup C disease in the UK: a success story. *Vaccine* **20 Suppl 1** S58-67.

Ohlsson A and Lacy JB (2004) Intravenous immunoglobulin for preventing infection in preterm and/or low-birth-weight infants. *Cochrane Database Syst Rev*(1): CD000361.

Peltola H, Safary A, Kayhty H *et al.* (1985) Evaluation of two tetravalent (ACYW135) meningococcal vaccines in infants and small children: a clinical study comparing immunogenicity of O-acetyl-negative and O-acetyl-positive group C polysaccharides. *Pediatrics* **76**(1): 91-6.

Perrett KP, Snape MD, Ford KJ *et al.* (2009) Immunogenicity and immune memory of a nonadjuvanted quadrivalent meningococcal glycoconjugate vaccine in infants. *Pediatr Infect Dis J* **28**(3): 186-93.

Pfister RE, Aeschbach V, Niksic-Stuber V *et al.* (2004) Safety of DTaP-based combined immunization in very-low-birth-weight premature infants: frequent but mostly benign cardiorespiratory events. *J Pediatr* **145**(1): 58-66.

Pourcyrous M, Korones SB, Arheart KL *et al.* (2007) Primary immunization of premature infants with gestational age <35 weeks: cardiorespiratory complications and C-reactive protein responses associated with administration of single and multiple separate vaccines simultaneously. *J Pediatr* **151**(2): 167-72.

Ramsay M, Kaczmarski E, Rush M *et al.* (1997) Changing patterns of case ascertainment and trends in meningococcal disease in England and Wales. *Commun Dis Rep CDR Rev* **7**(4): R49-54.

Rosenstein NE, Perkins BA, Stephens DS *et al.* (2001) Meningococcal disease. *N Engl J Med* **344**(18): 1378-88.

Schulzke S, Heininger U, Lucking-Famira M *et al.* (2005) Apnoea and bradycardia in preterm infants following immunisation with pentavalent or hexavalent vaccines. *Eur J Pediatr* **164**(7): 432-5.

Snape MD, Perrett KP, Ford KJ *et al.* (2008) Immunogenicity of a tetravalent meningococcal glycoconjugate vaccine in infants: a randomized controlled trial. *JAMA* **299**(2): 173-84.

Southern J, Borrow R, Andrews N *et al.* (2008) Immunogenicity of a reduced schedule of meningococcal group C conjugate vaccine given concomitantly with a 7-valent pneumococcal conjugate vaccine and a combination DTaP5/Hib/IPV vaccine in healthy UK infants. *Clin Vaccine Immunol*.

Southern J, Crowley-Luke A, Borrow R *et al.* (2006) Immunogenicity of one, two or three doses of a meningococcal C conjugate vaccine conjugated to tetanus toxoid, given as a three-dose primary vaccination course in UK infants at 2, 3 and 4 months of age with acellular pertussis-containing DTP/Hib vaccine. *Vaccine* **24**(2): 215-9.

Steven N and Wood M (1995) The Clinical Spectrum of Meningococcal Disease. In: Cartwright K (ed.) *Meningococcal disease*. Chichester, UK: John Wiley & Sons, p 177-206.

Thorburn K, Baines P, Thomson A *et al.* (2001) Mortality in severe meningococcal disease. *Arch Dis Child* **85**(5): 382-5.

Trotter CL, Andrews NJ, Kaczmarski EB *et al.* (2004) Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. *Lancet* **364**(9431): 365-7.

Trotter CL, Fox AJ, Ramsay ME *et al.* (2002) Fatal outcome from meningococcal disease - an association with meningococcal phenotype but not with reduced susceptibility to benzylpenicillin. *J Med Microbiol* **51**(10): 855-60.

Trotter CL and Gay NJ (2003) Analysis of longitudinal bacterial carriage studies accounting for sensitivity of swabbing: an application to Neisseria meningitidis. *Epidemiol Infect* **130**(2): 201-5.

Zuckerman JN (2000) The importance of injecting vaccines into muscle. Different patients need different needle sizes. *BMJ* **321**(7271): 1237-8.