

Meningococcal C vaccine (Meningitis C)

Factsheet

This fact sheet has been produced to provide background information on meningococcal disease and the vaccines available for prevention of this disease. It will concentrate primarily on the new meningococcal C (MenC) conjugate vaccine that is to be introduced in autumn 1999.

What is meningococcal disease?

Meningococcal disease results from a bacterial infection caused by the organism *Neisseria meningitidis*. This bacterium may cause both endemic and epidemic disease¹. The route of transmission is through droplets or respiratory secretions (e.g. coughing and sneezing), or more directly through kissing¹. Transmission from person to person requires either frequent or close prolonged contact. Nasopharyngeal carriage of meningococci is unusual in infants and young children². However, up to 25% of adolescents and 5-11% of adults naturally carry the bacteria without manifesting any signs or symptoms of the disease (known as carriers). What triggers the disease to develop in a susceptible person is unknown.

There is a marked seasonal variation in meningococcal disease rates, with peak levels in the winter months usually declining to low levels by late summer³. There are at least 13 serogroups of meningococcal disease known¹. Of these, there are only 2 serogroups, Groups B and C, which are of major importance in the UK. These groups account for almost all the cases in the UK. Other serogroups of meningococcal disease which occur much less frequently include A, Y, W-135, 29E and Z.

What are the signs and symptoms of meningococcal disease?

There are two types of meningococcal illness that most commonly occur: meningitis (inflammation of the membranes surrounding the brain (meninges)) and septicaemia (blood poisoning). In the case of septicaemia, this may occur alone or as part of an attack of meningitis. The most common signs and symptoms of meningitis and septicaemia are listed below. It is important to note that not all the symptoms listed may occur and may be slightly different in different age groups. In the early stages of the infection, the symptoms can be mild and similar to those of flu such as vomiting, fever, severe headache, arthralgia (painful joints) and stiff neck. In babies, additional symptoms may be seen such as a high-pitched moaning cry, refusing to eat, and difficulty wakening. However, as the disease progresses, photophobia (dislike of light), disorientation and reduced awareness possibly leading to coma may develop. Development of red

or purple spots (resembling bruising) that do not fade under pressure (do The Glass Test) is serious, indicating septicaemia and must be treated immediately with antibiotics. The Glass Test is done by pressing the side of a glass firmly against the rash to see if the rash fades and loses colour under pressure. If it does not change colour, parents should contact a doctor immediately.

Signs and symptoms of meningitis and septicaemia

Early stages of infection:

- Fever
- Stiff neck
- Severe headache
- Pain in back or joints
- Vomiting
- A high pitched, moaning cry (babies)
- Difficult to wake (babies)
- Refusal to eat (babies)
- Pale or blotchy skin (babies)

Latter stages of infection:

- Dislike of bright lights (photophobia)
- Reduced awareness/drowsiness (which may lead to a coma)
- Bruise-like rash that doesn't fade under pressure.

Both meningitis and septicaemia are very serious and must be treated immediately. Septicaemia occurs less frequently but is associated with higher mortality and morbidity.

How common is the disease?

Meningococcal infection is relatively rare affecting approximately 5 in 100,000 people a year in the UK. *Haemophilus influenzae* type b (Hib) used to be the commonest cause of meningitis in young children. Since the introduction of Hib immunisation in 1992 Hib meningitis has nearly disappeared in this country⁴. Similarly, introduction of MMR vaccine has led to a dramatic reduction in the number of cases of mumps meningitis⁴. Meningococcal infection is now the most common infectious cause of death in children and young people up to the age of 20 years. It is also the commonest cause of death overall in children aged 1-5 years⁵.

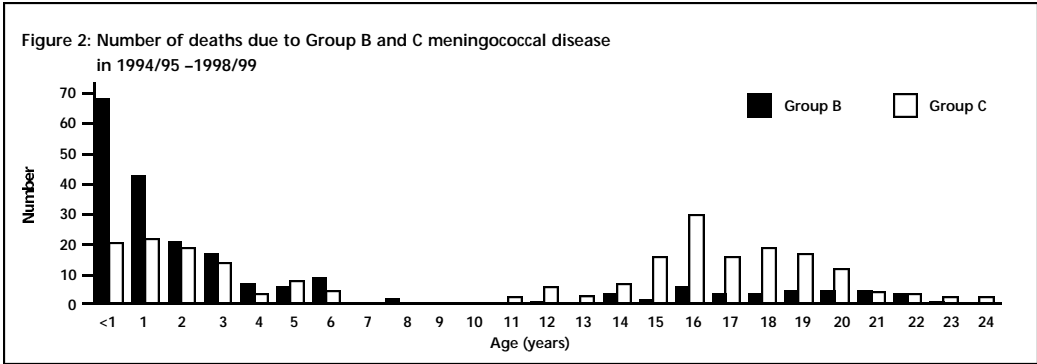
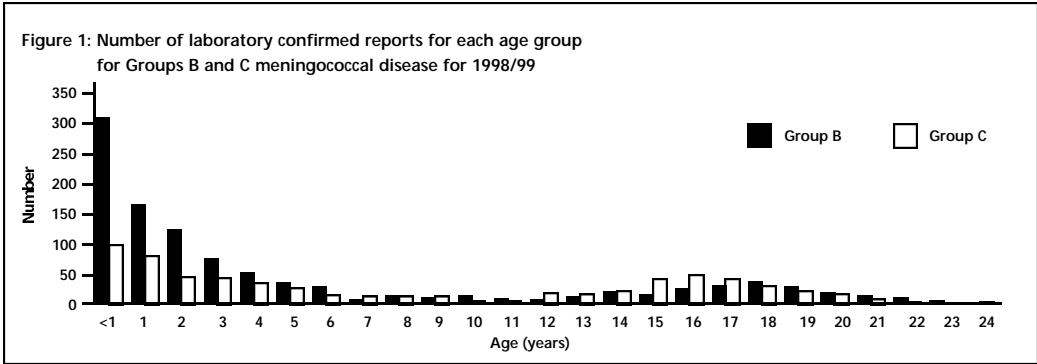
The peak incidence of meningococcal disease occurs in infants under 1 year of age when the infant's maternal protective antibodies have disappeared and the infant's active immunity has not developed⁶. Active immunity develops as bactericidal antibodies are acquired possibly through exposure to *Neisseria lactima*, a non-pathogenic (not causing disease) meningococcus and other related bacteria that express surface antigens in common with meningococci⁷.

Group B and C disease account for almost all cases in the UK. Group B disease has accounted for about 60% of cases with Group C accounting for about 30% of cases. However, over the last 5 years the pattern of meningococcal disease has changed. The proportion of Group C cases has risen to around 40%. There has been an overall increase in the number of laboratory confirmed cases of meningococcal disease. In 1994/95 the number of notifications of meningococcal disease was 1555 compared to 2962 in 1998/99 (provisional). These figures relate to epidemiological years which run from 1 July to 30 June. Whilst some of the increase may be due to improvements in reporting it is likely that there has also been a real increase with a larger increase in Group C disease. One particular serotype, Group C2a has been responsible for the most recent outbreaks in the UK. Outbreaks due to this serotype have previously been reported in Canada⁸ and North America⁹.

Who is at greatest risk?

The highest risk group for meningococcal disease is the under 1s, with the 1-5 age group following closely. The next highest risk group is young people aged 15-19 years. The number of laboratory confirmed cases for each age group (up to 20 years of age) for Groups B and C disease for the last year is shown in Figure 1. Group B disease accounts for the majority of cases in children under the age of 5, particularly in the under 2s. In contrast, Group C disease is more common in older children and adolescents. Figure 1 (see below) highlights the importance of Group C disease in the older age groups, particularly in teenagers and young adults¹⁰.

Individuals with underlying complement deficiencies are also at an increased risk of developing meningococcal disease. In these individuals, the infections tend to be due to the more uncommon serotypes e.g. Y and W-135, and are milder and the mortality rate is lower¹¹. Similarly, after splenectomy patients develop meningococcal disease more frequently than would be expected⁷. In contrast, individuals receiving chemotherapy for leukaemia or lymphoma² or those with HIV infection¹² do not appear to be at a significantly higher risk of developing meningococcal disease.



What are the mortality and morbidity associated with meningococcal disease?

Overall, approximately 1 in 10 people who develop meningococcal disease will die¹³. The death rate for septicaemia (20%) is substantially higher than for meningitis (7%)⁸. Of those who survive, approximately 25% report a reduced quality of life¹⁴. The most common long-term effects are skin scars, hearing loss, seizures, limb amputation(s), and brain damage¹.

The number of deaths in each age band over the last 5 years (shown in Figure 2) shows that in children under 5 years of age (particularly the under 2s) Group B disease accounts for around 70% of meningococcal deaths. In contrast, in the older age group, between about 15-20 years of age, Group C disease is the major cause of death. In this age group, Group C disease accounts for around 80% of deaths due to meningococcal infection.

Isn't there a vaccine already available?

Yes, there is a polysaccharide vaccine currently available which gives limited protection against Groups A and C disease. This type of vaccine is produced by purifying the polysaccharide from the capsule of the organism. Whilst this vaccine has been shown to be 75-90% effective in older children and adults, it does not protect infants under 2 years of age¹⁵, where the risk of infection is particularly high. This is one of the major drawbacks of this vaccine. This vaccine does not induce long-term memory and only confers protection for a short period of time, up to 3-5 years. Additionally, on revaccination some individuals may have a reduced response (termed hyporesponsiveness)¹⁶. It also has no effect on carriage of the organism. These are the main reasons why this vaccine is unsuitable for routine immunisation, especially in infants and young children.

What is the new conjugate vaccine?

The new meningococcal C conjugate vaccine uses the same technology that was applied to the development of the Hib conjugate vaccine. Whilst the vaccine is new, the constituents of the vaccines are not and have been used for a number of years. The polysaccharide and carrier proteins have been used separately in other vaccines safely in millions of doses. The technique called conjugation involves attaching a carrier protein to the polysaccharide antigen formed from the coat of the bacteria. The carrier proteins used in the new MenC conjugate vaccines are a non-toxic derivative of diphtheria toxin (CRM₁₉₇) or tetanus toxoid. The resultant vaccine induces a T-cell dependent antibody response and immunological memory, and is immunogenic in children

under 2 years of age¹⁷. This vaccine therefore, overcomes the limitations of the currently available polysaccharide vaccine.

How safe and effective is the new vaccine?

In addition to the safety and efficacy studies manufacturers are required to do for licensure, there have been a number of other additional studies carried out in the UK and abroad. In this country, studies have been carried out by the Public Health Laboratory Services (PHLS) in infants, toddlers, and school children specifically designed to study the performance of MenC conjugate vaccine in UK children. These studies have shown the vaccines to be safe and effective in all age groups. To date, more than 6,000 children and young people in the UK, and over 21,000 children, adults and young people outside the UK have already received these vaccines without any ill effects.

What does this vaccine protect against?

The MenC conjugate vaccine protects selectively against Group C disease and does not protect against any other type of meningococcal infection. It does not protect against Group B disease which is common in the UK, so it is important to have a high awareness of the signs and symptoms of the disease (refer to page 1 of this fact sheet).

Who will get the new vaccine?

Immunisation with MenC vaccine will become part of the routine Childhood Immunisation Programme in the UK. This vaccine will be given at the same time as primary immunisation with DTP, Hib and polio. Each infant will receive 3 doses given at 2, 3 and 4 months of age.

Introduction of the MenC conjugate vaccine is dependent on the licensure, availability and supply of the new conjugate vaccine. As the supply of vaccines will initially be limited, this vaccine is being introduced in stages according to the availability of the vaccine. Similarly, the groups being immunised have been selected according to the risk of disease, vaccine supply and whether a child is already being called up for another routine immunisation. Details of the groups being immunised and the number of doses of vaccine being given are listed in the table below. The number of doses of vaccine given will be dependent on age. Infants under 5 months of age will receive 3 doses and infants aged between 5 and 12 months (inclusive) will receive 2 doses. One dose of vaccine will be adequate in children greater than 12 months of age and adults.

Table 1: Summary of stages of introduction of MenC conjugate vaccine

Stage	Target group	Dose of vaccine	Setting	How called up
1 (from Autumn 1999)	Babies 2, 3 and 4 months	3	GP	DTP, Hib, polio call up
	Children 13 months	1	GP	MMR call up
	School children (year 11 and 6th form) aged 15 to 17 years	1	School/6th form college/ college of further education	Special programme
	Babies 5 to 12 months ¹	2	GP	Special appointments
2 (from January 2000)	Children 14 months to 5 years	1	GP	Special appointments
	Children 5 to 14 years ²	1	School	Special programme

¹ At present (October 1999), this group is likely to receive vaccine in January and February 2000. However, if vaccine becomes available before then they will be brought forward.

² At present (October 1999), this group is likely to start receiving vaccine in the summer school term.

What types of reactions are likely to be seen?

In the studies mentioned above no serious adverse effects were seen and the vaccine was well tolerated in all age groups. The most common reactions seen were redness and swelling at site of injection, mild fevers, irritability, and headaches. The frequency of these reactions (expressed as a percentage) for each age group are shown in Table 2. The rates of local reactions and systemic reactions are similar to those seen with Hib vaccine. The rate of systemic reactions with MenC conjugate was no higher than the background rates of other routinely administered vaccines at those ages. The rates of local reactions such as redness and swelling appear to increase with age. Systemic reactions such as fever are less common than local reactions in all age groups.

This vaccine has also been given safely to children with chronic medical conditions including asthma, eczema, congenital heart disease, epilepsy and renal conditions.

Can this vaccine be given with other vaccines?

Yes, the results of the studies have shown that this vaccine can be safely given with routine childhood immunisations including DTP/Hib, MMR, DT, Td and oral polio vaccine. There are no studies to date on hepatitis B or BCG vaccine being administered at the same time although there is no reason to suspect an interaction. BCG has been given within a month of MenC vaccine with no adverse effects. This vaccine does not affect the seroconversion rate of other vaccines administered at the same time as, before or after MenC vaccine^{17,18}.

Table 2: Most common reactions seen after immunisation with MenC conjugate vaccine

Age group	Local reactions	Systematic reactions
Infants (<12 months)	• Redness (>3cm) (2–4%)	• Irritability (about 50%) • Fever (2–4%)
Toddlers (12–17 months)	• Redness (>3cm) (2–3%)	• Irritability (19%) • Fever (5%)
Primary school children (4–11 years)	• Redness (>3cm) (29%)	• Fever (1.1%) • Headaches (10%)
Secondary school children (12–18 yr)	• Redness (>3cm) (26%)	• Fever (2.5%) • Headaches (14%)

Can an infant's immune systems cope with another vaccine?

Yes. There is no evidence that multiple vaccinations overload a child's immune system. Evidence supporting the safety of giving multiple vaccinations at the same time comes from a study by Chen et al, 1998¹⁹. In this study, different combinations of multiple vaccines including Hib, DTP and polio were given to around 18,000 infants up to the age of 11 months. The results of this study showed that there was no increase in the number of hospital visits after any of the combinations of vaccines, even where infants were immunised against up to 8 diseases, in comparison to giving polio alone. This study also showed that multiple vaccinations given simultaneously could be given safely to children aged between 12 and 23 months of age. In the studies performed in the UK, MenC conjugate has been given safely in combination with one or more of the following vaccines, DTP/Hib, polio, DT/Td and MMR. These studies showed that the infant's immune system could cope with the additional vaccination and that there was no increase in the number of reactions seen.

Can everyone be given this vaccine?

No, immunisation is contraindicated in individuals who have had a hypersensitivity reaction to any constituent of the vaccine including meningococcal C polysaccharide, diphtheria toxoid or the CRM₁₉₇ carrier protein, or tetanus toxoid. Immunisation should be postponed in individuals who have an acute febrile illness or high fever.

Can this vaccine be administered to pregnant women?

Although there is no evidence to suggest that this vaccine is not safe in pregnancy, it should not be given unless there is a high risk of the individual developing meningococcal C disease such as in an outbreak, or a close contact of a recent case. Similarly, it is not routinely recommended in women breastfeeding.

Can individuals who have previously been vaccinated with the old vaccine still be immunised with the new conjugate vaccine?

Yes, this vaccine can be given after receiving the polysaccharide vaccine. It is advisable to leave a 6 month gap to ensure a good response but may be given sooner in certain situations such as in an outbreak, or a close contact of a recent case.

How will the effect of vaccination be monitored?

Since January 1998 surveillance of meningococcal disease has been enhanced to improve the information available from routine data sources (which underestimate the true incidence of disease). The aim of this system is to increase the proportion of clinically diagnosed cases which is confirmed and grouped to allow accurate distinction between Group B and C disease. Laboratory confirmation of cases of C disease will allow the identification of individuals who have been immunised and who subsequently develop meningococcal disease, that is where the vaccine fails to protect. All cases of Group C disease in the groups who are eligible for immunisation will therefore be followed up to monitor the impact of immunisation.

What should parents do if their child becomes unwell after receiving meningococcal C vaccine?

If a parent has any concerns about the health of their child after they have been immunised, particularly if they become seriously unwell, they should be encouraged to consult a doctor. It may be that the child is suffering from an illness that is totally unrelated to the vaccine.

If a doctor, nurse or pharmacist suspects an adverse reaction to any vaccine, he/she can report this to the Committee on Safety of Medicines (CSM), using the Yellow Card spontaneous reporting scheme. The new MenC conjugate vaccine is a black triangle (▼) product. This means **all** suspected adverse reactions must be reported to the CSM. For the polysaccharide meningococcal vaccine only **serious** adverse reactions need be reported.

What to do if a parent suspects meningococcal disease?

If a parent suspects that their child has meningococcal infection (refer to page 1 for signs and symptoms), they should contact a doctor immediately or take them to the nearest casualty department.

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