MENINGOCOCCAL C VACCINE (MENINGITIS C)

Facts for healthcare professionals
This booklet 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 Ireland in Autumn 2000. It is based on material which was prepared by Health Promotion England and the Department of Health, England, which we wish to acknowledge.

This document has been developed by an expert committee and reviewed by the following organisations:

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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 disease. The route of transmission is through droplets or respiratory secretions (e.g. coughing and sneezing), or more directly through kissing. Transmission from person to person requires either frequent or close prolonged contact. Nasopharyngeal carriage of meningococci is unusual in infants and young children. 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 summer. There are at least 13 serogroups of meningococcal disease known. Of these, there are only two serogroups, Groups B and C, which are of major importance in Ireland. These groups account for almost all the cases in Ireland. 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 waking. 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 Tumbler Test) is serious, indicating septicaemia and must be treated immediately with antibiotics. The Glass Tumbler 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 15 in 100,000 people a year in Ireland. *Haemophilus influenzae type b* (Hib) used to be the commonest cause of meningitis in young children. Since the introduction of Hib immunisation in October 1992 Hib meningitis has nearly disappeared in this country. Meningococcal infection is the most common infectious cause of death in children and young people up to the age of 20 years.

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 developed. Active immunity develops as bactericidal antibodies are acquired possibly through exposure to *Neisseria lactima*, a non-pathogenic (not causing disease) neisseria, and to other related bacteria that express surface antigens in common with meningococci.

Group B and C disease account for almost all cases in Ireland. Group B disease accounts for about two thirds of cases with Group C accounting for about one third of cases. However, over the last 3 years the pattern of meningococcal disease has changed. The proportion of Group B cases has risen from 54% in 1997 to 66% in 1999. There has been an overall increase in the number of laboratory confirmed cases of meningococcal disease, with 343 cases being identified in 1997, 368 cases in 1998 and 435 cases in 1999. 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 B disease.

Not all cases of invasive meningococcal disease are laboratory confirmed. An enhanced surveillance scheme that combines clinical and laboratory findings is in place to capture all cases, whether definitively diagnosed or not. In 1997 the number of cases of meningococcal disease detected by enhanced surveillance was 448, in 1998 it was 448 and in 1999 this had risen to 535 cases.
Who is at greatest risk?

The highest risk group for meningococcal disease is the under 1s, with the 1 to 6 year age group following closely. The next highest risk group is young people aged 15 to 18 years. The number of laboratory confirmed cases for each age group (up to 25 years of age) for Groups B and C disease for 1997 to 1999 year are shown in Figure 1. Group B disease accounts for the majority of cases in children under the age of 6. In contrast, Group C disease is relatively more common in adolescents. Figure 1 (see below) highlights the importance of Group C disease in the older age groups, particularly in teenagers and young adults.

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 lower. Similarly, after splenectomy patients develop meningococcal disease more frequently than would be expected. In contrast, individuals receiving chemotherapy for leukaemia or lymphoma or those with HIV infection do not appear to be at a significantly higher risk of developing meningococcal disease.

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**Figure 1. Number of Laboratory-Confirmed Cases of Group B and C Meningococcal Disease in Ireland, 1997-99**

![Graph showing number of cases by age group](image)
What are the mortality and morbidity associated with meningococcal disease?

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

The number of deaths in each age band over the last 3 years (shown in Figure 2) shows that Group B disease accounts for 83% of deaths in children under 1 year, 92% of deaths in children aged 1 to 4 years and 50% of deaths in children aged 5 to 9 years. In contrast, in the older age group, between 15 and 19 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.

Figure 2. Number of Deaths due to Group B and C Meningococcal Disease in Ireland, 1997-99
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 age\textsuperscript{13}, 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)\textsuperscript{14}. 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 (MenC) 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 (CRM\textsubscript{197}) 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 age\textsuperscript{15}. This vaccine therefore, overcomes the limitations of the currently available polysaccharide vaccine.
How safe and effective is the new vaccine?

Meningococcal C conjugate vaccine was first introduced in clinical trials in 1994. Approximately 8000 infants, children and young adults were immunised in clinical trials in the UK. Over 20,000 infants, children and young adults have been immunised in trials in other countries (USA, Canada, Holland). These studies showed an excellent immune response in all age groups with evidence of long-term protection, that vaccine was well tolerated and no serious side effects were found. In clinical trials, the vaccine has been shown to be >98% immunogenic after three doses in babies at 2, 4 and 6 months, and a single dose of vaccine in subjects over 12 months has also been shown to be highly immunogenic.

Up to June 2000, approximately 13.5 million doses of meningococcal C conjugate vaccine have been distributed in the UK, and there have been 4764 reports of suspected adverse reactions to meningococcal C vaccine, a rate of less than 1 in 10,000. The majority of reactions were non serious and the children recovered quickly and without complications. A causal relationship between seizures (frequency of approximately 1 in 100,000 distributed doses) and meningococcal C vaccination has not been established. It is likely that many of the reported seizures were faints, many of the reports of late onset seizures were co-incidental and convulsions in infants were likely to be febrile convulsions. Although symptoms of meningism such as neck pain/stiffness or photophobia have been reported, there is no evidence that the vaccine causes meningococcal C meningitis. Clinical alertness to the possibility of co-incidental meningitis should therefore be maintained.

What does this vaccine protect against?

The Men C 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 Ireland, 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). It does not protect against Group A disease which is the most common strain associated with foreign travel.
Who will get the new vaccine?

Immunisation with Men C vaccine will become part of the routine Childhood Immunisation Programme in Ireland. This vaccine will be given at the same time as primary immunisation with DTaP, Hib and polio. This vaccine is being introduced in phases. The groups being immunised have been selected according to the risk of disease and whether the child has already been called up for another routine immunisation. The first phase will commence from Autumn 2000 and the second/third phases will follow when the first has been completed.

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 1 year of age will receive 3 doses, similar to Hib immunisation. One dose of vaccine will be adequate in children greater than 12 months of age and adults. MenC vaccine cannot be mixed with other vaccinations in the same syringe, and so infants will receive 3 separate injections at the 2, 4 and 6 month visit.

Health professionals are advised to take the opportunity to check the vaccine status of children under 5 years and vaccinate simultaneously with MMR if indicated.
Table 1:
Summary of phases of introduction of Men C conjugate vaccine

<table>
<thead>
<tr>
<th>Phase</th>
<th>Target Group</th>
<th>Dose of vaccine</th>
<th>Setting</th>
<th>How called up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Babies 2, 4 &amp; 6 mths</td>
<td>3</td>
<td>GP</td>
<td>DtaP Call-Up</td>
</tr>
<tr>
<td></td>
<td>Babies 6-12 mths</td>
<td>3</td>
<td>GP</td>
<td>Special Programme</td>
</tr>
<tr>
<td></td>
<td>Children 15 mths</td>
<td>1</td>
<td>GP</td>
<td>MMR Call-Up</td>
</tr>
<tr>
<td></td>
<td>Children 13 mths - 4 yrs</td>
<td>1</td>
<td>GP</td>
<td>Media Campaign</td>
</tr>
<tr>
<td>From Autumn 2000</td>
<td>School children 15-18 yrs</td>
<td>1</td>
<td>School</td>
<td>Special Programme</td>
</tr>
<tr>
<td>and</td>
<td>Those aged 15-18 yrs</td>
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<td>College/</td>
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<td></td>
<td>not in full-time education</td>
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<td>Training</td>
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<td>Centres</td>
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<tr>
<td>Phase 2</td>
<td>Children 5-6 yrs</td>
<td>1</td>
<td>School</td>
<td>Consent Form sent home to parents/guardians of junior infants</td>
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<tr>
<td>On completion of Phase 1</td>
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<tr>
<td>Phase 3</td>
<td>Children 7-14 yrs</td>
<td>1</td>
<td>School</td>
<td>Consent Form sent home to parents/guardians of remaining classes in primary and secondary schools</td>
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<tr>
<td>On completion of Phase 2</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Those 19-22 yrs</td>
<td>1</td>
<td>GP</td>
<td>Media campaign advising to attend GP</td>
</tr>
</tbody>
</table>

How is the vaccine given?

The vaccine is given by intramuscular injection, preferably in the anterolateral thigh in infants and in the deltoid region in older children, adolescents and adults.
What types of reactions are likely to be seen?

There have been very rare reports of allergic reactions including anaphylactoid reactions following administration of meningococcal C vaccine. Recovery is usually rapid. In all age groups injection site reactions (including redness, swelling and tenderness/pain) are very common. However, these are not usually clinically significant. Redness or swelling of at least 3cm and tenderness interfering with movement for more than 48 hours are infrequent where studied. Fever of at least 38.0°C is frequent, but does not usually exceed 39.1°C particularly in older age groups.

Although symptoms of meningism such as neck pain/stiffness or photophobia have been reported there is no evidence that the vaccine causes meningococcal C meningitis. Clinical alertness to the possibility of coincidental meningitis should therefore be maintained.

There have been very rare reports of seizures following meningococcal vaccination, individuals have usually rapidly recovered. Some of the reported seizures may have been fainted. The reporting rate of seizures was below the background rate of epilepsy in children. In infants seizures were usually associated with fever and were likely to be febrile convulsions.

Older children and teenagers:

Nausea, vomiting, rash, malaise, lymphadenopathy, headache and myalgia have been reported. Dizziness and fainted have also been reported, however these types of reactions are common after injection with any vaccine.

Infants and toddlers:

Symptoms including crying, irritability, drowsiness, impaired sleeping, anorexia, diarrhoea and vomiting were common after vaccination but there was no evidence that these are related to meningococcal C vaccine rather than concomitant vaccines particularly DTP.

If a doctor, nurse or pharmacist suspects an adverse reaction to any vaccine, he/she can report this to the Irish Medicines Board (IMB), using the Yellow Card spontaneous reporting scheme. All suspected adverse reactions must be reported to the IMB.
Can this vaccine be given with other vaccines?

The meningococcal C conjugate vaccine can be given at the same time as other vaccines but must not be mixed. This vaccine can be safely given with routine childhood immunizations including DtaP, Hib, HBV, MMR, DT, Td and oral polio vaccine. There are no studies to date on 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 meningococcal C 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 meningococcal C vaccine15,17.

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, 199816. In this study, different combinations of multiple vaccines including Hib, DTP and polio were given to around 18,000 infants up 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 CRM 197 carrier protein, or tetanus toxoid, e.g. anaphylaxis, fever greater than or equal to 40.5°C within 48 hours of vaccine administration for which no other cause was found, or any of the following occurring within 72 hours of vaccines administration: prolonged unresponsiveness; prolonged inconsolable or high pitched screaming for more than 4 hours; convulsions or acute encephalopathy. Immunisation should be postponed in individuals who have an acute febrile illness or high fever.

While HIV infection is not a contraindication, meningococcal C vaccine has not been specifically evaluated in the immunocompromised. Meningococcal C vaccine has not been evaluated in persons with thrombocytopenia or bleeding disorders. The risk versus benefit for persons at risk of hemorrhage following intramuscular injection must be evaluated.
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 1997 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 Irish Medicines Board (IMB), using the Yellow Card spontaneous reporting scheme. All suspected adverse reactions must be reported to the IMB.

What to do if a parent suspects meningococcal disease?

If a parent suspects that their child has meningococcal infection (refer to page 3 for signs and symptoms), they should contact a doctor immediately or take them to the nearest casualty department.
The following individuals were involved in developing this document

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www.meningitis.ie
References


5. Dr. Jerry Fogarty, personal communication


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