Meningococcal vaccines

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SYNOPSIS

In Australia, most cases of invasive meningococcal disease are caused by *Neisseria meningitidis* serogroup B for which there is currently no vaccine. Serogroup C infection comprises about one third of cases, but its incidence varies between the states and between age groups. Serogroup A rarely occurs in Australia. Polysaccharide vaccines which give short-term protection against serogroups A, C, W135 and Y have been available for many years. These vaccines are mainly used for travellers to regions where serogroup A and W135 infections are prevalent, but they can also be used in outbreak control. The new conjugated serotype C vaccines are highly effective, have a low rate of adverse events and induce immunologic memory. They will be used in mass vaccination programs in Australia from 2003, but they only protect against serotype C infection.

Index words: meningitis, immunisation.

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Introduction

Each year in Australia, meningococcal infections cause 700–800 hospitalisations and 35–40 deaths (10 in children aged 0–4 years). Invasive disease usually presents as meningitis or septicaemia. The mortality is high and those who survive may have severe sequelae.[1,2]

Epidemiology

The causative organism (*Neisseria meningitidis*) is carried asymptomatically by about 20% of the population.[1,2] It is spread by the respiratory route. In Australia in 2001 the incidence of meningococcal disease was about 3.5 cases per 100 000 population, but the rate in indigenous people is nearly six times higher. People with inherited defects of properdin or complement, or functional or anatomic asplenia, are at increased risk of meningococcal infection. The highest attack rate is in children aged 0–4 years and young adults 15–24 years. In Australia, there is a distinct seasonality with peak incidence in winter and spring.[1,2] The course of the illness is often rapid and dramatic.

Microbiology

Neisseria meningitidis has 13 serogroups.[2] Within a serogroup there are often many serotypes and subtypes identifiable by differences in outer membrane proteins. The serogroups currently responsible for most invasive disease internationally are A, B, C, W135 and Y.

In Australia serogroup B causes most infections and serogroup C about one third of cases (Fig. 1). However, an increase in the rate of serogroup C infections has been noted over the past seven years. There are marked differences in serogroup C rates from state to state, with New South Wales and Victoria experiencing the largest recent increases.[3] The number of notifications of serogroup C disease exceeded the number of notifications of serogroup B disease in Victoria in 2000 and 2001 (Fig. 2).[4] Increasing rates of serogroup C infection have also been seen in the UK and North America.

Serogroup A disease has rarely been seen in Australia since a small outbreak in the early 1990s, but occurs regularly in Africa and Asia. Serogroup W135 has recently been seen in Africa and in pilgrims to the Hajj. New Zealand has been experiencing an outbreak of serogroup B disease since 1991 with rates of type B disease nearly 10 times higher than those reported in Australia.[5]

Vaccines

There are two quite different types of meningococcal vaccines. The multivalent polysaccharide vaccine (containing polysaccharides from serogroups A, C, W135, Y) has been available for many years. It is frequently used in adults and older children travelling to endemic areas of Africa and Asia. The new conjugated serogroup C vaccine is effective in young children.

Fig. 1

Meningococcal cases per year – Australian estimates
(estimates for 1997–2001)

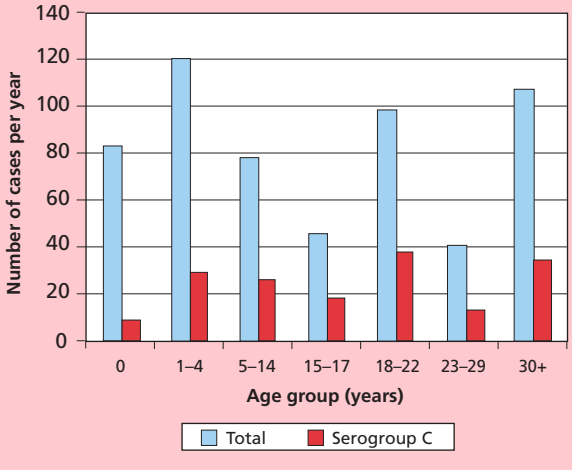
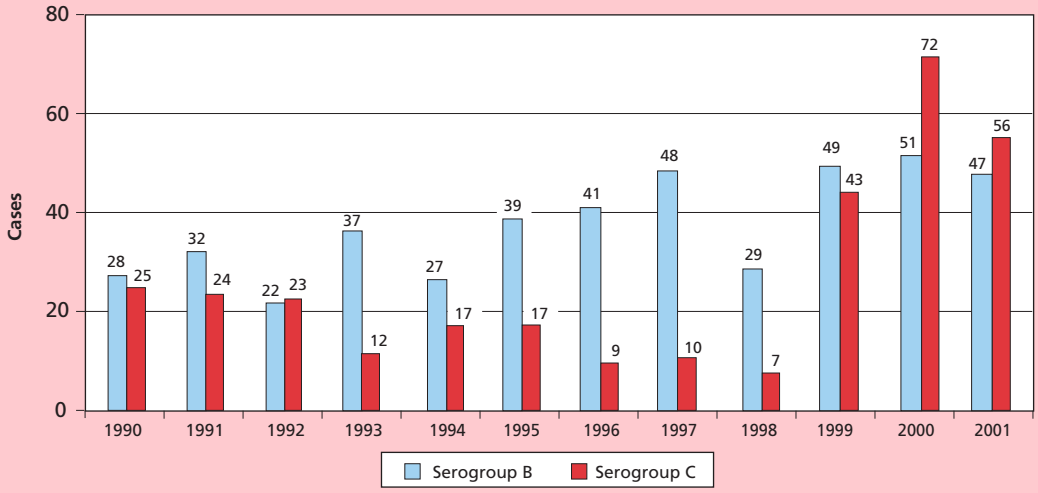


Fig. 2

Serogroup B & C meningococcal infection in Victoria, 1990–2001



There is no vaccine for serogroup B. A prototype vaccine especially developed for the subtype (B:4:P1.7b,4) prevalent in New Zealand is currently being studied in Auckland.[5]

Meningococcal tetravalent polysaccharide vaccine

There are two products available (Mencevax ACWY – containing phenol 0.25% as a preservative, and Menomune – containing thiomersal 0.01% as a preservative). Each protects against serogroups A, C, W135 and Y. These vaccines are provided in a monodose vial with 0.5 mL saline diluent.[2] They do not contain infectious material.

These tetravalent polysaccharide vaccines can be used for travellers and in outbreak control although the conjugated vaccine would be preferred for control of serogroup C outbreaks. Polysaccharide vaccines are not suitable for mass vaccination programs because:

- children under the age of 10 years have a diminished immunologic response and the vaccines are not approved for use in children under the age of two years
- immunity persists for only 3–5 years depending on the age of the recipient
- hyporesponsiveness occurs following subsequent doses
- effectiveness against serogroup C disease varies according to age and length of follow-up (one study showed 65% effectiveness for two years in people aged six months–20 years).

Adverse events such as injection site reactions and fever, which occur in 2% of children, are usually mild. Contraindications are hypersensitivity to any of the vaccine components or anaphylactic reaction following a previous dose.[2]

Meningococcal serogroup C conjugate vaccine

There are three products available:

- Meningitec – the 0.5 mL dose contains group C oligosaccharide conjugated to 15 microgram of non-toxic *Corynebacterium diphtheriae* CRM_{197} protein + aluminium phosphate adjuvant
- Menjugate – the 0.5 mL dose contains group C polysaccharide conjugated to 12.5–25 microgram of a non-toxic *Corynebacterium diphtheriae* CRM_{197} protein + aluminium hydroxide adjuvant
- NeisVac-C – the 0.5 mL dose contains group C polysaccharide conjugated to 10–20 microgram of tetanus toxoid + aluminium hydroxide adjuvant.

These vaccines contain no infectious material and have some important features:

- they can be given to all age groups including infants from the age of six weeks
- only a single dose is required for people over one year old (babies under the age of four months require three doses at least one month apart; those aged over four months but less than 12 months old require two doses*)
- the effectiveness is about 90% in the short term[6,7]
- they may have a long duration of protection – possibly 15 or more years.

Adverse event rates vary with the age of the child. Children under the age of two years can develop local redness (2%), irritability (20–50%) and fever more than 38°C (2–5%). Older children more frequently develop local redness (30%) and headaches (10–14%), but have a slightly lower rate of fever (1–2%).[3,6]

The vaccines are contraindicated in people with a hypersensitivity to any of the components or an anaphylactic reaction to a previous dose. They are not recommended in pregnancy (Category 2B) due to lack of data.

The vaccines may be administered simultaneously with other vaccines in the Australian Standard Vaccination Schedule. They should not be mixed in the same syringe with other vaccines.

* The National Health and Medical Research Council (NHMRC) recommends two doses, but this conflicts with the product information which recommends three doses in this age group. The NHMRC recommendations should be followed.

Meningococcal serogroup C vaccination programs

A mass vaccination program using conjugated meningococcal C vaccines began in the UK in November 1999.[6] The program offered vaccine progressively to everyone aged less than 18 years and there has been a very high uptake (80%). The UK program has resulted in a reduction of at least 75% in serotype C disease in the vaccinated age groups. While there is evidence of herd immunity in these age groups, there has been no evidence of herd immunity in other age groups.[6,7]

The Australian Government has announced approval for a meningococcal C vaccination program to commence in 2003. The conjugated vaccine has been included in the Australian Standard Vaccination Schedule for all children reaching the age of one year. In 2003 the vaccine will also be offered in a catch-up program to children aged one to five years by general practitioners and to senior high school children in a school-based program. In 2004–05 the remaining school-age children will have the opportunity to receive the vaccine in school-based programs. The rapidity of implementation of school-based programs will vary between jurisdictions. In view of the excellent response to the Measles Control Campaign, these school-based programs are likely to be popular.

The community must understand that this program will only prevent serogroup C disease. It will take several years to make a significant impact on group C disease and the 200 cases and 18 deaths which group C infection causes nationally each year (Fig. 1).

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 71)

3. The currently available conjugate meningococcal vaccines do not protect against serogroup B infection.
4. Most cases of meningitis in Australia are caused by *Neisseria meningitidis* serogroup C.

Book review

Therapeutic Guidelines: Gastrointestinal. Version 3.
Melbourne: Therapeutic Guidelines Limited: 2002. 208 pages.
Price (including GST and postage): $38.75, students $31.05, RACGP members $35.45.

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Firstly, the format in a small soft cover book is useful. It doesn't fit into any pocket that I have, but is easy to toss into a briefcase or the back of the car. It is the sort of book that one might refer to at the time of a difficult problem, but it is also useful to read when one can snatch a few minutes.

The book begins in a similar format to other guidelines with a chapter devoted to 'Getting to know your gastrointestinal drugs'. This is often a good starting place and worth a read. It serves as a good summary for points to remember when prescribing these medications.

The most useful aspects for general practice seem to be the topics on the more nebulous aspects of medicine. I found it useful to peruse the chapters on 'Oral disorders', 'Common disorders of vitamin and mineral metabolism', 'Constipation', 'Diarrhoea', 'Irritable bowel syndrome' and 'Perianal disorders'.

There are several good tables such as Table 12 which shows the recommended daily intakes for various vitamins. You can compare these recommendations with the contents of the common vitamin preparations listed in the table.

Other tables of interest included the comparison table for commonly used laxatives, lactose content of infant formulae and milk products as well as a comparison table for infant rehydration formula.

At the end of the book, there is a section about gastrointestinal drugs in pregnancy and breastfeeding. While I suspect that many of my colleagues would now find this information on a computer, it is useful to know that it can be found here too. There is also a handy list of support groups for the case manager in us; very useful when accreditation comes around.

The other chapters read more like a textbook, but give comprehensive coverage of gastrointestinal issues. These include topics like oesophageal disorders, peptic ulcers, pancreatic disorders, hepatitis, liver disorders, small bowel disorders and inflammatory bowel disease. There is a good summary on how to manage enteral nutrition and stomas, although I find it rare if the patient or their carer does not know more about the problem than I do.