Vaccines for Preventing Meningococcal Disease
Prof. Tony Walls, University of Otago, New Zealand
A Webber Training Teleclass

Vaccines for preventing meningococcal disease

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Outline

• Meningococcal disease
  – Clinical features
  – Epidemiology
• New Zealand meningococcal epidemic
• Meningococcal vaccines
  – MeNZB™ in New Zealand
  – MenAfrivac™
  – Conjugate meningococcal vaccines
  – The future of meningococcal vaccines

Invasive meningococcal disease

Carriage and transmission

• Asymptomatic carriage provides reservoir for transmission
• Increasing carriage with age
  – Up to 25% in 15-19 year olds
• Risk factors:
  – Overcrowding, Hajj pilgrimage, students at university, exposure to *N. meningitidis*, specific immune deficiencies

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Epidemiology

Table 1
Invasive meningococcal incidence by country or region.

<table>
<thead>
<tr>
<th>Country/region</th>
<th>Incidence/100,000</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>African meningitis belt</td>
<td>10–1000 (during epidemics)*</td>
<td>Not applicable</td>
</tr>
<tr>
<td>New Zealand</td>
<td>2.4</td>
<td>2010</td>
</tr>
<tr>
<td>Australia</td>
<td>0.2</td>
<td>2009</td>
</tr>
<tr>
<td>Chile</td>
<td>0.5</td>
<td>2010</td>
</tr>
<tr>
<td>Argentina</td>
<td>0.6</td>
<td>2008</td>
</tr>
<tr>
<td>Canada</td>
<td>0.47</td>
<td>2008</td>
</tr>
<tr>
<td>United States</td>
<td>0.28</td>
<td>2009</td>
</tr>
</tbody>
</table>

* The annual incidence during serogroup A epidemics in the meningitis belt can exceed 10000 cases per 100,000 population.

Meningococcal serogroups

- 12 meningococcal serogroups
- Vast majority of infections are caused by six serogroups:
  - A, B, C, W135, X and Y

Meningococcal vaccines

- Serogroup specific
- Polysaccharide vaccines
- Protein-polysaccharide conjugate vaccines

Global distribution serogroups

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Pure polysaccharide vaccine

- Polysaccharide vaccine poorly immunogenic in children < 2 years of age

Conjugate protein-polysaccharide vaccines

Serogroup A Meningococcal disease

Number of meningitis deaths in African meningitis belt

Serogroup distribution African meningitis belt

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Halperin et al., 2012 Vaccine;30S:B26

Serogroup

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of samples tested</th>
<th>Meningococcal serogroup</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Serogroup A</td>
</tr>
<tr>
<td>2007</td>
<td>2533</td>
<td>609</td>
</tr>
<tr>
<td>2008</td>
<td>5413</td>
<td>1092</td>
</tr>
<tr>
<td>2009</td>
<td>5688</td>
<td>1966</td>
</tr>
<tr>
<td>2010</td>
<td>4132</td>
<td>439</td>
</tr>
<tr>
<td>2011*</td>
<td>4278</td>
<td>197</td>
</tr>
</tbody>
</table>

* The proportion of cases investigated varied between countries and from year to year but was usually about 10%.

www.meningitis.org
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- Collaboration between:
  - Bill & Melinda Gates Foundation
  - Path (Seattle based NGO)
  - World Health Organisation
- Meningococcal A vaccine developed by Serum Institute of India Ltd
  - MenAfriVac™

- Single dose conjugate vaccine administered to 1-29 year olds
- Cost US$0.40 per dose
- Burkina Faso 10-day national campaign and over 11.4 million people vaccinated
- www.meningvax.org

- MVP News Digest 2012
  - "to date, not a single case of group A Meningitis has been notified in more than 54 million individuals who received the MenAfriVac™ in 2010-11."

- Global distribution serotypes

- New Zealand experience

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Group B meningococcal vaccines

- No licensed serogroup B polysaccharide vaccine
  - Poor immunogenicity
  - Possible induction of autoantibodies
- Outer membrane vesicle (OMV) vaccines developed for clonal outbreaks
  - Chile, Brazil, Cuba, Norway

Outer membrane vesicles

Figure 3. Electron micrographs of Neisseria meningitidis A and outer membrane vesicles B.

A meningococcal strain is depicted (A), arrow denotes only outer layer of the outer membrane.

New Zealand

Fig. 4 Meningococcal disease by age group and ethnicity, average annual rate for 1996–2000. (C) European; (H) Maori; (P) Pacific Island people; (I) other.

Baker et al., 2002 J Paediatr Child Health 37:115

THE NEW ZEALAND MEDICAL JOURNAL
Vol 117 No 1200 ISSN 1175 8716

The New Zealand Meningococcal Vaccine Strategy: A tailor-made vaccine to combat a devastating epidemic

Kerry Sexton, Diana Lennon, Philipp Oster, Sus Croughle, Dianne Martin, Kim Mulholland, Tessa Pericival, Stewart Reid, Joanna Stewart, Jane O’Hillahan

Abstract

The New Zealand Meningococcal Vaccine Strategy aims to end the devastating 14-year epidemic of B:4:P:16R:P4 group B meningococcal disease in New Zealand through a mass immunisation programme to all under 20-year-olds using a tailor-made vaccine (MenNZB™). This paper describes the rationale, development, and key components of the New Zealand Meningococcal Vaccine Strategy. A summary of the efficacy and safety data of existing outer membrane vesicle group B meningococcal vaccines is included as these data critically support the Strategy.
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Meningococcal B vaccines

4CMenB vaccine
- A new vaccine with recombinant proteins and outer membrane vesicles
- Developed by reverse vaccinology
- Each dose contains:
  - 50ug NadA
  - 50ug fHbp
  - 50ug NHBA
  - OMV from NZ98/254

4CMenB vaccine
- Not yet licensed
- Phase II studies show immunogenicity in infants and adolescents
- Can be given safely with other infant vaccines
- Potential to cover 78% of serogroup B isolates

Global distribution serogroups

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Other meningococcal vaccines

- Polysaccharide vaccines
  - Mencevax ACWY
  - Menommune ACYW
- Conjugate vaccines
  - Meningitec (Group C)
  - NeisVac-C (Group C)
  - Menactra (Quadrivalent A,C,Y and W135)
  - Menveo (Quadrivalent A,C,Y and W135)

Men C vaccine in the UK

- Men C vaccination introduced into UK 1999
- 3-dose schedule at 2, 3 and 4 months

Men C vaccine in the UK

Men C disease in Canada

Quadravalent Meningococcal vaccine

- Ideal for countries where meningococcal disease caused by several serogroups
- Cost implications

- January 2011 Advisory Committee on Immunization Practice (ACIP) recommended:
  - Vaccinate persons aged 2-55 years at increased risk of meningococcal disease
  - Vaccinate all adolescents 11 to years
  - All adolescents receive a booster at age 16 years

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Summary

• Meningococcal disease is preventable
• New vaccines in development
  – e.g. Meningococcal B vaccines
• Global initiatives for resource poor countries
• Introduction of Meningococcal vaccines into routine schedules will depend on many different factors:
  – Rates of disease, cost, acceptability