Immunization Update
& focus on meningococcal vaccine
PART 2

Gregory Hussey
Vaccines for Africa Initiative
Institute of Infectious Diseases
University of Cape Town

www.vacfa.uct.ac.za
Meningococcal Disease in South Africa
Incidence of Meningococcal Disease

African Meningitis Belt cases 1970 - 2010

http://www.who.int/gho/epidemic_diseases/meningitis/en/
http://www.path.org/menafrivac/meningitis-belt.php
Meningococcal carriage rates are low during infancy and peak at 19 Years of Age\textsuperscript{1}

- Young adults are the most common source of transmission to the community\textsuperscript{2}
- Up to 10\% of adolescents and adults are asymptomatic transient carriers\textsuperscript{3}

\textsuperscript{1}Christensen H. \textit{Lancet Infect Dis}. 2010;10(12):853;
\textsuperscript{2}Pelton SI. \textit{Pediatr Infect Dis J}. 2009;28(4):329;
\textsuperscript{3}CDC. In: \textit{Epidemiology and Prevention of Vaccine-Preventable Diseases. (The Pink Book.)} 12th ed. 2012.
## Clinically significant serogroups

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>Characteristics</th>
</tr>
</thead>
</table>
| A         | • Leading cause of epidemic meningitis worldwide  
           | • Most prevalent serogroup in Africa and China  
           | • Rare in Europe and the Americas |
| B         | • Major cause of endemic disease in Europe and the Americas  
           | • No vaccine available |
| C         | • Major cause of endemic disease in Europe and North America  
           | • Multiple outbreaks in schools and communities |
| Y         | • Associated with pneumonia, particularly in the elderly  
           | • Increased during the 1990s in the United States  
           | • Has become more common among infants and adolescents in recent years |
| W-135     | • Small percentage of infections worldwide  
           | • Outbreaks associated with Hajj pilgrims starting in 2000 |
Global *Neisseria meningitidis* Serogroup Distribution Has Been Varied, Making Trends Unpredictable

Represents serogroups not defined for each individual country


*Slide courtesy of Novartis*
MenW has become the predominant cause of meningococcal disease

South Africa, 1999–2012

*May include serogroups e.g., X, E, Z, or non-groupable; †Serogroup not identified; ‡Year spans August through July.

Serogroup data from viable isolates and PCR results


Slide adapted from Novartis
Number of cases of laboratory-confirmed meningococcal disease in South Africa reported to GERMS-SA by month and year, 2003 to 2012 (n=4537)

Ackn: AvG, NICD
Incidence of invasive meningococcal disease by age category, South Africa, 2003 to 2012 (n=4308, age unknown for 229 cases)

Ackn: AvG, NICD
Case-fatality ratio of invasive meningococcal disease by age category, South Africa, 2003-2012 (n=1560)

Ackn: AvG, NICD
HIV prevalence among patients with invasive meningococcal disease, 2003-2012 and population HIV prevalence, 2012, South Africa

MCD risk in patients with AIDS.
Harris CM et al
Open Forum Inf Diseases 2016

Incidence of MCD in AIDS patients 25 to 64 years olds was 3.5 cases per 100000 person years (95% confidence interval [CI], 2.1–5.6), compared with 0.3 cases per 100000 person years (95% CI, 0.3–0.3) for persons of the same age group not reported to have AIDS (relative risk = 12.9; 95% CI, 7.9–20.9).


Ackn: AvG, NICD
Meningococcal vaccine development – time line

Holst et al. Human Vaccines & Immunotherapeutics 9:6, 1241–1253; June 2013
<table>
<thead>
<tr>
<th>Property</th>
<th>Polysaccharide</th>
<th>Conjugate</th>
</tr>
</thead>
<tbody>
<tr>
<td>T cell–dependent response</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Immune memory</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Persistence of protection</td>
<td>No</td>
<td>Yes(^a)</td>
</tr>
<tr>
<td>Booster effect</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Reduction of carriage</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Herd immunity</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
## Conjugate vaccines

<table>
<thead>
<tr>
<th>Serogroups</th>
<th>Manufacturer</th>
<th>Age indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monovalent</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mengitec</td>
<td>MenC-CRM Pfizer</td>
<td>≥ 2 Months</td>
</tr>
<tr>
<td>Menjugate</td>
<td>MenC-CRM Novartis</td>
<td>≥ 2 Month</td>
</tr>
<tr>
<td>NeisVac-C</td>
<td>MenC-TT Baxter</td>
<td>≥ 2 Months</td>
</tr>
<tr>
<td>MenAfrivac</td>
<td>Men A-TT Serum Institute India</td>
<td>1 – 29 years</td>
</tr>
<tr>
<td><strong>Combination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MenHibrix</td>
<td>Hib-MenCY-TT GSK</td>
<td>6 wks – 18 mths</td>
</tr>
<tr>
<td>Mentinorix</td>
<td>Hib-MenC-TT GSK</td>
<td>6 wks – 18 mths Booster 1-2 yrs</td>
</tr>
</tbody>
</table>
## Conjugate vaccines

<table>
<thead>
<tr>
<th>Quadrivalent</th>
<th>Serogroups</th>
<th>Manufacturer</th>
<th>Age indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menveo</td>
<td>MenACWY-CRM</td>
<td>Novartis 2013</td>
<td>2-55 yrs (1 dose) 7-23 mths (2 doses) 2 Mths (4 doses)</td>
</tr>
<tr>
<td>Nimenrix</td>
<td>MenACWY-CRM</td>
<td>GSK Pfizer 2016</td>
<td>≥ 12 Month (1 dose)</td>
</tr>
<tr>
<td>NmVac4</td>
<td>MenACWY-DT</td>
<td>JN Int Med Corp</td>
<td>≥ 9 Months?</td>
</tr>
<tr>
<td>Menactra</td>
<td>MenACWY-DT</td>
<td>SP 2014</td>
<td>2-55 yrs (1 dose) 9-23 mths (2 doses)</td>
</tr>
</tbody>
</table>
MenC Conjugate


Ireland – MenC in 2000; infants were given three doses before 1 year of age, with a catch-up programme in adolescents. 2013, NIP – 3 doses: 3 months (MenC), 12–13 months (Hib & MenC), and 14–15 years (Men C)

England and Wales - MenC introduced in 1999, with a catch up campaign in children up to 19 years of age. NIP - two dose schedule at 3 and 12 months of age.

Andrews & Pollard - LID2014;14: 426–34
Effect of a serogroup A meningococcal conjugate vaccine (PsA–TT) on serogroup A meningococcal meningitis and carriage in Chad: a community trial


Summary

Background A serogroup A meningococcal polysaccharide–tétanos toxoid conjugate vaccine (PsA–TT, MenAfriVac) was licensed in India in 2009, and pre-qualified by WHO in 2010, on the basis of its safety and immunogenicity. This vaccine is now being deployed across the African meningitis belt. We studied the effect of PsA–TT on meningococcal meningitis and carriage in Chad during a serogroup A meningococcal meningitis epidemic.
**Impact of MenA vaccine in Chad.** Dougla et al. *Lancet* 2013

![Graph showing incidence of meningitis in Chad](image_url)

**Figure 3: Incidence of reported cases of meningitis in Chad, 2009–12**

Vaccination with PsA–TT was undertaken in patients aged 1–29 years at the end of 2011 (arrow).  
PsA–TT=serogroup A meningococcal polysaccharide–tetanus toxoid conjugate vaccine.

Caroline L Trotter, Clément Lingani, Katya Fernandez, Laura V Cooper, André Bita, Carol Tewi-Benissan, Olivier Ronceaux, Marie-Pierre Préziou, James M Stuart

Summary
Background In preparation for the introduction of MenAfriVac, a meningococcal group A conjugate vaccine developed for the African meningitis belt, an enhanced meningitis surveillance network was established. We analysed surveillance data on suspected and confirmed cases of meningitis to quantify vaccine impact.

Figure: Total annual suspected and confirmed cases of bacterial meningitis across all nine countries in relation to MenAfriVac introduction (dotted line)
MenAfriVac® breaks the cold chain barrier!

19 February 2014—A study published online today in the Journal Vaccine shows that removing the pioneering vaccine from constant refrigeration is not only safe but could extend vaccination coverage to the remotest regions in sub-Saharan Africa.

A second study published in the Bulletin of the World Health Organization shows that cutting out the cold chain could halve storage and vaccine transportation costs.

MenAfriVac®, which is manufactured by Serum Institute of India Ltd., is the first vaccine allowed to travel outside of the cold chain in Africa. As shown in the above photograph, there are no ice packs in the vaccine box, and a peak threshold indicator tells the vaccinators if the vaccine has reached its limit and needs to be discarded.
Serogroup B vaccines

- Bexsero® (Novartis) & Trumenba® (Pfizer)
- USA – routinely used for 10-23 year olds. 2 dose regimen.
- Bexsero® was introduced into the routine UK schedule on 1st September 2015. The vaccine is given at 2 and 4 months, with a booster at 12 months.
Meningococcal vaccines registered in SA

• Currently there are 2 types of meningococcal vaccines available in South Africa
  – A polysaccharide vaccine (Menomune®, Sanofi Pasteur (MPSV4))
  – A protein-conjugate polysaccharide vaccine (Menactra®, Sanofi Pasteur (MCV4)).

• These are both quadrivalent vaccines targeting the polysaccharide capsules of serogroups A, C, W and Y.
Recommendations for the use of meningococcal vaccines in South Africa

Susan Meiring*, Gregory Husseyb, Prakash Jeenac, Salim Parkerd and Anne von Gottgbergd

aDivision of Public Health Surveillance and Response, National Institute for Communicable Diseases, a division of the National Health Laboratory Services, Johannesburg, South Africa
bVaccines for Africa Initiative, Institute for Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa
cDepartment of Paediatrics, University of KwaZulu-Natal, Durban, South Africa
dGeneral Practitioner, South African Society of Travel Medicine, Cape Town, South Africa
centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, a division of the National Health Laboratory Services, Johannesburg, South Africa
*Corresponding author, email: susan.meiring@nhrs.ac.za

Background: Although meningococcal disease (MD) incidence in South Africa is low, Neisseria meningitidis (NM) causes severe disease that is often life-threatening and can cause long-term disabilities. A quadrivalent protein-conjugated meningococcal vaccine (MCV4) is available, and provides protection against 75% of disease causing serogroups in South Africa.

Recommendations: We advise vaccination of persons at high risk of meningococcal disease including those with complement deficiency and asplenia; laboratory personnel from reference laboratories who work with NM; and travellers to Saudi Arabia. The need for routine vaccine against meningococcal disease in South Africa is controversial given the current burden of disease. However, due to the high morbidity/mortality of MD we recommend that clinicians consider vaccination of healthy infants and children; HIV-infected persons with a CD4 count > 25%; students attending college/university/military academies; and miners.

Conclusion: Protein-conjugated meningococcal vaccine is preferable to the polysaccharide vaccine given the ability of the protein-conjugated meningococcal vaccine to induce immune memory, allow for booster responses and eliminate carriage of the organism in the person vaccinated.

Keywords: guidelines, meningitis, meningococcal vaccines, Neisseria meningitidis, South Africa, vaccine
## MCV recommendations - 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Recommendation</th>
<th>Doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hajj pilgrims and travellers to Saudi</td>
<td>Required</td>
<td>Single primary dose</td>
<td>A booster dose every 3 years for MPSV4 or 5 years for MCV4 is required for repeated travel as per current Saudi regulations</td>
</tr>
<tr>
<td>Travellers to meningitis belt or other areas where disease is hyperendemic/epidemic</td>
<td>Recommended</td>
<td>Single primary dose</td>
<td>Booster dose every 5 years should be considered for repeated travel to highly endemic areas</td>
</tr>
<tr>
<td>Research/reference laboratory workers routinely exposed to N. meningitidis</td>
<td>Recommended</td>
<td>Single primary dose</td>
<td>Booster dose every 5 years if risk remains</td>
</tr>
<tr>
<td>Persons with medical conditions at high risk of acquiring infection: Complement component deficiencies and asplenic conditions</td>
<td>Recommended</td>
<td>Two-dose primary schedule 12 weeks apart</td>
<td>Booster dose every 5 years</td>
</tr>
</tbody>
</table>
## MCV recommendations – 2
Should be considered

<table>
<thead>
<tr>
<th>Population group</th>
<th>Primary dosing</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy children and infants</td>
<td>Children 9 months to 23 months: 2 doses 12 weeks apart</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children ≥24 months: 1 dose</td>
<td></td>
</tr>
<tr>
<td>Healthy adolescents or young adults entering university or college (particularly if staying in hostels)</td>
<td>Single dose prior to entry into university or college</td>
<td></td>
</tr>
<tr>
<td>Military recruits on training or deployment</td>
<td>Single dose prior to commencing training or deployment</td>
<td>Booster dose required if risk remains high 5 years after primary dose</td>
</tr>
<tr>
<td>Miners</td>
<td>Single primary dose</td>
<td></td>
</tr>
<tr>
<td>Attendees of mass gatherings</td>
<td>Single primary dose</td>
<td></td>
</tr>
<tr>
<td>HIV infection</td>
<td>Two-dose primary schedule 12 weeks apart</td>
<td>Booster every 5 years</td>
</tr>
<tr>
<td>Other immunocompromising conditions</td>
<td>Two-dose primary schedule 12 weeks apart</td>
<td>Booster every 5 years</td>
</tr>
</tbody>
</table>
Menactra & GBS

Does Menactra Meningococcal Conjugate Vaccine cause Guillain-Barré Syndrome (GBS)? NO

No. Two large studies were conducted to investigate whether GBS was caused by the vaccine or was coincidental with vaccination. These studies included a combined total of over 2 million vaccinated adolescents. The results of these studies showed that there was no link between Menactra and GBS.

- A 2012 study used health records of over 9.6 million preteens and teens to evaluate a possible link between Menactra and GBS. The study found that youth who received Menactra were not at increased risk of developing GBS.
- Another large 2012 study combined the above study with data from the Vaccine Safety Datalink to search for diagnoses of GBS in 11.2 million preteens and teens who received Menactra. This study also found no link between GBS and Menactra and observed 0 confirmed GBS cases.

Note: A 2003 study concluded that people who received the 1976 swine influenza vaccine had a small increased risk for developing GBS.

https://www.cdc.gov/vaccinesafety/concerns/history/gbs-menactra-faqs.html
CIOMS/WHO cause specific definition of AEFIs

1. **Vaccine product-related reaction**
   - An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.

2. **Vaccine quality defect-related reaction**
   - An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer.

3. **Immunization error-related reaction**
   - An AEFI that is caused by inappropriate vaccine handling, prescribing or administration.

4. **Immunization anxiety-related reaction**
   - An AEFI arising from anxiety about the immunization.

5. **Coincidental event**
   - An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.
What adverse effects do vaccines or immunisation cause?

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common &gt; 1% and &lt; 10%</td>
<td>Rare &gt;0.01% and &lt; 0.1%</td>
</tr>
<tr>
<td>Expected</td>
<td>Unexpected</td>
</tr>
</tbody>
</table>

**Examples**

| Fever ISR # Rash | Febrile convulsion BCG adenitis ISR - Abscess Urticaria/Angioedema | Thrombocytopenia Hypotonic hyporesponsive episodes (HHE) Anaphylaxis |

# ISR - Injection Site Reaction
- The Global Advisory Committee on Vaccine Safety (GACVS) was established in 1999 to respond promptly, efficiently, and with scientific rigour to vaccine safety issues of potential global importance.

- The Committee provides independent, authoritative, scientific advice to WHO on vaccine safety issues of global or regional concern with the potential to affect in the short or long term national immunization programmes

http://www.who.int/vaccine_safety/committee/en/
14TH ANNUAL AFRICAN VACCINOLOGY COURSE

The popular Annual African Vaccinology Course (AAVC) convened by VACFA will take place in November 2018

Who should attend?
- Immunisation program managers & officers
- Researchers & public health professionals working in the field of vaccines (immunology, immunisation activities such as advocacy, policy formulations, etc.)
- Postgraduate students & postdocs in the field of vaccinology/immunology

Applications are now open: www.vacfa.uct.ac.za

Topics to be covered during the 5-day course include:

- Programmatic challenges on immunisation
- Basic epidemiology & immunology
- Surveillance, monitoring & reporting of AEFI
- Underused, new & future vaccines, session on NITAGs
- Media engagement on immunisation
- Web-based training in vaccinology

News

Monday, 18 June 2018

South Africa recommends the use of meningococcal vaccines

Among certain groups, there is a significant morbidity/mortality of meningococcal disease in South Africa. The authors recommend that clinicians consider vaccination of healthy infants and children; HIV-infected persons with a CD4 count < 25%; students attending college/ university/military academies; and miners.

Read more