Global Burden of Meningococcal Disease

Prof. David Salisbury CB FRCP FRCPCH FFPH FMedSci.
Centre for Global Health Security, Chatham House, London.
Neisseria meningitidis

- Gram negative diplococci.
- Ten percent of adults carry N. meningitidis in oropharynx.
- A, B, C, W135, X, Y account for most disease.
- A Sub-Saharan Africa, B temperate climates, C outbreaks.
- Epidemics in Africa, Asia, Europe, Americas, N.Zealand.
- The annual number of invasive disease cases worldwide is estimated to be at least 1.2 million, with 135,000 deaths related to invasive meningococcal disease
Global epidemiology of invasive meningococcal disease.

Categorisation of countries by risk of meningococcal disease.

**HIGH:**
Countries with $>10$ cases/100,000 population) and/or $>1$ epidemic over the last 20 years.

**MODERATE:**
Countries with 2–10 cases/100,000 population per year.

**LOW:**
Countries with $<2$ case/100,000 population per year.

Classification based on country-specific epidemiological data with pre-defined cutoffs of high, moderate, and low endemicity categories as used by the WHO’s Strategic Advisory Group of Experts on Immunizations (SAGE) in its recently updated recommendations on the use of meningococcal vaccines.

Categorisation of countries by risk of meningococcal disease: **HIGH.**

**AFRICA:**
Angola, Benin, Burkina Faso, Burundi, Cameroon, CAR, Chad, Cote Ivoire, Ethiopia, Gambia, Ghana, Guinea, Guinea Bissau, Kenya, Mali, Mauretania, Namibia, Niger, Nigeria, RD Congo, Rwanda, Senegal, Tanzania, Togo, Uganda.

**EASTERN MEDITERRANEAN:**
Sudan, Saudi Arabia.

**EUROPE:**
NONE.

**AMERICAS:**
Uruguay.

**SOUTH EAST ASIA:**
NONE

**WESTERN PACIFIC:**
Mongolia, New Zealand.
This categorisation may be right for outbreaks in previous 20 years, it is WRONG for current rates of disease.

Following the devastating epidemic of 1996–1997 (with more than 250,000 cases of disease and over 25,000 deaths), African leaders called for the development of a vaccine that would eliminate, once and for all, group A meningitis epidemics in Africa.

In all, the MenAfriVac campaigns reached more than 63 million individuals in 2014, bringing the total number of vaccinees in the African meningitis belt to more than 217 million in 15 countries since vaccine launch in 2010 (Benin, Burkina Faso, Cameroon, Chad, Côte d’Ivoire, Ethiopia, The Gambia, Ghana, Mali, Mauritania, Niger, Nigeria, Senegal, Sudan, and Togo).

Not a single case of MenA meningitis among over 100 million people in 10 African countries that the global partnership has vaccinated.

You cannot trust meningococci to behave themselves!
Serogroup X, previously a rare cause of sporadic meningitis, has been responsible for outbreaks between 2006 and 2010 in Kenya, Niger, Togo, Uganda, and Burkina Faso, the latter with at least 1,300 cases of serogroup X meningitis among the 6,732 reported annual cases.

Somali mothers waiting in line in Mogadishu to have their babies vaccinated against meningitis and other diseases in 2013. **Meningitis C** infections are on the rise across Africa. Credit Ben Curtis/Associated Press
Rate of meningococcal disease (per 100,000 population), by year — United States, 1970–2011

Base-case Cost per QALY* saved by Vaccine Cost in Thousands US$

* Excluding indirect cost from deaths
Estimates from Monte Carlo Simulation
Incidence data include 18% adjustment for underreported cases
Deaths from Meningococcal disease by age, 1994 – 1999, E & W.
Laboratory Confirmed Cases of Serogroup C Meningococcal Disease
England & Wales - Cumulative Cases aged 15 to 17 years old

- Cumulative Cases 1998/1999
- Cumulative Cases 1999/2000
- Cumulative Cases 2000/2001 (to week 2001/20)

Immunisation with serogroup C conjugate vaccine in 15 - 17 yr olds began on 1 November 1999

no of cases
0  10  20  30  40  50  60  70  80  90  100  110  120  130  140  150

week no (totals from mid-year)
Reduction in Men C incidence in **unvaccinated groups** by age  
*(Ramsay et al, BMJ 2003)*

<table>
<thead>
<tr>
<th>Age scheduled for MCC</th>
<th>Rate per 10^5 pre-MCC campaign</th>
<th>Rate per 10^5 post MCC campaign</th>
<th>% Reduction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-17 yrs</td>
<td>5.3</td>
<td>1.79</td>
<td>66 (37 to 82)</td>
</tr>
<tr>
<td>11 to 14 yrs</td>
<td>5.54</td>
<td>1.11</td>
<td>80 (46 to 93)</td>
</tr>
<tr>
<td>9-10 yrs</td>
<td>1.69</td>
<td>1.30</td>
<td>23 (-228 to 82)</td>
</tr>
<tr>
<td>5-8 yrs</td>
<td>2.07</td>
<td>0.87</td>
<td>58 (-35 to 87)</td>
</tr>
<tr>
<td>2 to 4 yrs</td>
<td>3.94</td>
<td>1.20</td>
<td>70 (30 to 87)</td>
</tr>
<tr>
<td>1 yr</td>
<td>6.82</td>
<td>2.05</td>
<td>70 (-24 to 93)</td>
</tr>
<tr>
<td>infant catch-up</td>
<td>7.49</td>
<td>1.56</td>
<td>79 (-54 to 97)</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>4.08</strong></td>
<td><strong>1.36</strong></td>
<td><strong>67 (52 to 77)</strong></td>
</tr>
</tbody>
</table>
Introduction of Meningococcal C vaccine in the UK.

The graph shows the number of meningococcal C cases under 20 years old (pink triangles) and over 20 years old (blue triangles) from 1998 to 2010. The introduction of the Meningococcal C vaccine is indicated by an arrow. The cases significantly decrease after the introduction, with a notable drop in cases under 20 years old.
Figure 1
Cumulative number of laboratory-confirmed cases of invasive meningococcal group W (MenW) disease by epidemiological year, England, 2009/10–2014/15 (n=407)

Data for the most recent epidemiological year (2014/15) are complete until end May 2015.
Since the epidemiological year 2009/10, the United Kingdom has experienced a year-on-year increase in meningococcal group W (MenW) disease due to rapid expansion of a single endemic hyper-virulent strain belonging to sequence type 11 clonal complex (cc). This strain was identified among cases diagnosed across all regions and was not linked to travel abroad. Consequently, an adolescent MenACWY conjugate vaccination programme for 13-18 year-olds will be introduced in August 2015, with priority given to 17-18 year-olds (school leavers).

Figure 2

Age distribution of laboratory-confirmed cases of invasive meningococcal group W (MenW) disease by epidemiological year, England, 2009/10–2014/15 (n=407)

Data for the most recent epidemiological year (2014/15) are complete until end May 2015.
**Implications for other countries**

The rapid introduction of a MenACWY conjugate vaccination programme in the UK will provide direct protection for adolescents at the time when they are most vulnerable to IMD and, is expected consequently, to contribute to indirect (herd) protection by interrupting transmission through carriage prevention.

- So far, no other European country has reported an endemic increase in invasive MenW disease.
- In France, six epidemiologically- and geographically-unlinked MenW cases were diagnosed in the first three months of 2012 [14]. Unlike the situation in the UK, all cases were associated with recent travel by the patient or patient contacts to sub-Saharan Africa, where large multinational outbreaks of MenW:cc11 were occurring at the time.
- Given how quickly this hypervirulent MenW:cc11 clone has established itself in populations across different continents [8], European countries should remain highly vigilant and be prepared to control this aggressive but vaccine-preventable infection.
Teenagers will soon be vaccinated against deadly meningitis W after a steep rise in the number of cases, Public Health England has announced.

There were 22 confirmed cases in 2009, 117 last year and experts predict even more cases in the future.

Meningitis W also has a higher-than-usual death rate.

The government's Joint Committee on Vaccination and Immunisation called for 14 to 18-year-olds to be vaccinated "as soon as possible".
Teenagers going to university and college this year are being offered protection against a deadly strain of meningitis, called MenW.

GPs across the UK are inviting 17 and 18-year-olds to come for a vaccine. First-time students under 25 are eligible too.

Teenagers born between 1 September 1996 and 31 August 1997 will be sent an invitation by their GP to come and receive the vaccination. Over the next two years, 14 to 17-year-olds will also be contacted to be offered the MenACWY vaccine.
Number of cases of meningococcal disease over time in England and Wales. Principal data from Notifications of Infectious Disease (NOIDS) for England and Wales, with sections indicating diseases reported during different time periods.

Re-evaluating cost effectiveness of universal meningitis vaccination (Bexsero) in England: modelling study.  
Christensen H, Trotter CL, Hickman M, Edmunds WJ. BMJ. 2014 Oct 9;349:g5725. doi: 10.1136/bmj.g5725
In the short term, case reduction is greatest with routine infant immunisation (26.3% of cases averted in the first five years).

This strategy could be cost effective at £3 (€3.8, $4.9) a vaccine dose, given several favourable assumptions and the use of a quality of life adjustment factor.

If the vaccine can disrupt meningococcal transmission more cases are prevented in the long term with an infant and adolescent combined programme (51.8% after 30 years), which could be cost effective at £4 a vaccine dose.

Assuming the vaccine reduces acquisition by 30%, adolescent vaccination alone is the most favourable strategy economically, but takes more than 20 years to substantially reduce the number of cases.

Routine infant vaccination is the most effective short term strategy and could be cost effective with a low vaccine price.

Critically, if the vaccine reduces carriage acquisition in teenagers, the combination of infant and adolescent vaccination could result in substantial long term reductions in cases and be cost effective with competitive vaccine pricing.

Conclusions

- Meningococcal infections can be sporadic, endemic, epidemic.
- Epidemiology is constantly changing.
- Cases can just as easily decrease as increase.
- Criteria for vaccination are not applied consistently – public and political demand, burden of disease, cost effectiveness are all powerful drivers.
- Meningococci are not to be trusted to behave predictably.