Recent epidemiology of meningococcal disease and impact of immunisation programmes in the UK

Ray Borrow
ray.borrow@phe.gov.uk

21st June 2018, MRF, Bristol
More than £10,000 has been raised for the family who have been told their 10-month-old daughter will have all her limbs amputated.

Petition signed by more than 800,000 people calling for the meningitis B vaccine to be given to all children under 11.
Evolving UK meningococcal immunisation programme

- **Nov 1999**: UK first country to introduce MCC at 2, 3, 4 months of age with catch-up campaign
- **Sept 2006**: MCC programme changed to 3, 4 & 12 months of age
- **June 2013**: MCC programme changed to 3 & 12 months & 13/14 years of age
- **Sept 2015**: MCC changed to ACYW at 13/14 years of age & catch-up started for all 13 to 18 year olds
- **July 2016**: UK first country to introduce 4CMenB, 2, 4 & 12 months of age
- **3 month of age MCC removed**
Invasive meningococcal disease laboratory-confirmed cases England and Wales 1998/9 to 2017/18 (June 13th)

PHE MRU provisional data
UK MenB programme

Negotiations to procure at cost-effective price were concluded in late March 2015

MenB vaccine given with routine immunisation appointments from 1st September 2015

**Routine cohort:** infants born on or after the **1 July 2015**
**Schedule:** 2, 4 and 12 months (2+1)

**Catch-up cohort:** infants born from **1 May to 30 June 2015**
**Schedule:** 3, 4 and 12 months (2+1)
**Schedule:** 4 and 12 months (1+1)
Invasive Meningococcal Disease in <2 year-olds
England & Wales (2006/07-2010/11)
Assuming 88% of MenB strains covered by 4CMenB, then VE against vaccine-preventable strains ~94%
Vaccine eligible cohort update

Data until 31st December 2017

- A total of 202 laboratory confirmed cases of IMD in infants were born from May 1st 2015.

- MenB accounted for 135 (67%) of cases:

<table>
<thead>
<tr>
<th>B</th>
<th>W</th>
<th>C</th>
<th>Y</th>
<th>NG</th>
</tr>
</thead>
<tbody>
<tr>
<td>135</td>
<td>41</td>
<td>12</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>67%</td>
<td>20%</td>
<td>6%</td>
<td>4%</td>
<td>3%</td>
</tr>
</tbody>
</table>

- 25 infants were too young to receive 4CMenB (less than 2 months of age).

- Thus 177 infants/children were vaccine eligible:

<table>
<thead>
<tr>
<th>B</th>
<th>W</th>
<th>C</th>
<th>Y</th>
<th>NG</th>
</tr>
</thead>
<tbody>
<tr>
<td>116</td>
<td>40</td>
<td>11</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>66%</td>
<td>23%</td>
<td>6%</td>
<td>3%</td>
<td>2%</td>
</tr>
</tbody>
</table>
Results: Up to 31\textsuperscript{st} December 2017 (28 months of surveillance) for vaccine eligible children

- Of the MenB cases, 21 (18%), 48 (43%), 36 (31%), and 11 (9%) had received zero, one, two or three doses of vaccine, respectively.

- Cultures were received from 66 (57%) of the MenB cases and thus available for MATS analysis.

- A total of 50 MenB cases (43%) were confirmed by PCR only.
Culture confirmed MenB cases (n=66) - Potential 4CMenB coverage by number of doses

No doses
- Covered: 31 (47%)
- Not Covered: 20 (30%)
- Unknown: 5 (8%)

Three doses
- Covered: 10 (15%)
- Not Covered: 5 (8%)
- Unknown: 10 (15%)

Two doses
- Covered: 31 (47%)
- Not Covered: 20 (30%)
- Unknown: 5 (8%)

One dose
- Covered: 5 (55%)
- Not Covered: 10 (15%)
- Unknown: 5 (8%)

Culture confirmed MenB cases (n=66) - Potential 4CMenB coverage by number of doses
Non-culture MenB cases (n=50)

Potential coverage by PorA and/or fHbp

- **No doses**: 42%
  - PorA P1.4 and/or fHbp 1.1 or 1.4: 12%
  - Other PorA and other fHbp variant 1: 47%
  - Other PorA and fHbp variant 2 or 3: 35%
  - No product: 31%

- **One dose**: 35%
  - PorA P1.4 and/or fHbp 1.1 or 1.4: 12%
  - Other PorA and other fHbp variant 1: 35%
  - Other PorA and fHbp variant 2 or 3: 6%
  - No product: 31%

- **Two doses**: 16, 32%
  - PorA P1.4 and/or fHbp 1.1 or 1.4: 6%
  - Other PorA and other fHbp variant 1: 33%
  - Other PorA and fHbp variant 2 or 3: 12%
  - No product: 31%

- **Three doses**: 6, 12%
  - PorA P1.4 and/or fHbp 1.1 or 1.4: 17%
  - Other PorA and other fHbp variant 1: 33%
  - Other PorA and fHbp variant 2 or 3: 17%
  - No product: 31%
Cases in <1 year-olds
Cases in <15 to 24 year-olds
Vaccine Safety

- So far, 3 million doses given to children so far

- Concerns before vaccine introduction
  - ? Kawasaki Disease – very rare in <6m, no evidence of increase
  - ? Seizures – no evidence of increase in any kind of seizure
  - ? Less likely to have subsequent vaccination – no evidence (97-98% return for their subsequent vaccines)

- Primary Care consultations for fever
  - 1.5-fold increase in infants attending GP for fever post-vaccination with 4CMenB

- Secondary care consultations for fever
  - 3-4 fold increase in infants attending the ED for fever post-vaccination with 4CMenB

- Hospitalisations for fever
  - Around half the infants attending the ED have septic screens +/- antibiotics
  - ? Did the parents give prophylactic paracetamol as recommended?
### Effectiveness of Meningococcal B Vaccine against Endemic Hypervirulent *Neisseria meningitidis* W Strain, England

Shamez N. Ladhani, Marzia Monica Giuliani, Alessia Biolchi, Mariagrazia Pizza, Kazim Beebeejaun, Jay Lucidarme, Jamie Findlow, Mary E. Ramsay, Ray Borrow

<table>
<thead>
<tr>
<th>Lab number</th>
<th>Site</th>
<th>Type</th>
<th>Pre-</th>
<th>Pool1</th>
<th>Pool2</th>
<th>Pool3</th>
<th>Pool4</th>
</tr>
</thead>
<tbody>
<tr>
<td>M11-240417</td>
<td>CSF</td>
<td>W:2aP1.5,2 cc11</td>
<td>&lt;2</td>
<td>64</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
</tr>
<tr>
<td>M11-240427</td>
<td>Blood</td>
<td>W:2aP1.5,2 cc11</td>
<td>&lt;2</td>
<td>32</td>
<td>32</td>
<td>64</td>
<td>128</td>
</tr>
<tr>
<td>M11-240498</td>
<td>Blood</td>
<td>W:NT:P1.5,2 cc11</td>
<td>&lt;2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>M12-240016</td>
<td>Blood</td>
<td>W:2aP1.5,2 cc11</td>
<td>&lt;2</td>
<td>32</td>
<td>32</td>
<td>64</td>
<td>128</td>
</tr>
<tr>
<td>M11-240798</td>
<td>Blood</td>
<td>W:NT:P1.5,2 cc11</td>
<td>&lt;2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>M12-240754</td>
<td>Blood</td>
<td>W:NTP1.5,2 cc11</td>
<td>&lt;2</td>
<td>64</td>
<td>64</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
</tbody>
</table>

*Suggests that children immunised with 4CMenB may have some protection against MenW cc11*
Any Impact on W? (up to 2016/17)
Capsular group W in vaccine eligible cohort

No doses, 6 cases (3 culture & 3 PCR only)

One dose, 16 cases (13 culture & 3 PCR only)

Two doses, 17 cases (11 culture & 6 PCR only)

Three doses, 1 case (PCR only):

- onset 7 months post booster
- PorA P1.5,2
- fHbp variant 1, allele 377, peptide 318

W cc11 normally fHbp variant 2, allele 22, peptide 22

W cc11 isolates posses NadA variant 2/3
England & Wales lab confirmed cases of serogroup W

W cc11 split tree analysis
# MenACWY vaccination programme roll-out

## Table of Birth Cohorts and Vaccination Timelines

<table>
<thead>
<tr>
<th>Birth cohort</th>
<th>2014/15 year - age</th>
<th>Academic year</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/09/2003-31/08/2004</td>
<td>Y6 – 10/11</td>
<td></td>
</tr>
<tr>
<td>01/09/2002-31/08/2003</td>
<td>Y7 - 11/12</td>
<td></td>
</tr>
<tr>
<td>01/09/2001-31/08/2002</td>
<td>Y8 - 12/13</td>
<td></td>
</tr>
<tr>
<td>01/09/2000-31/08/2001</td>
<td>Y9 - 13/14</td>
<td></td>
</tr>
<tr>
<td>01/09/1999-31/08/2000</td>
<td>Y10 - 14/15</td>
<td></td>
</tr>
<tr>
<td>01/09/1998-31/08/1999</td>
<td>Y11 - 15/16</td>
<td></td>
</tr>
<tr>
<td>01/09/1997-31/08/1998</td>
<td>Y12 - 16/17</td>
<td></td>
</tr>
<tr>
<td>01/09/1996-31/08/1997</td>
<td>Y13 – 17/18</td>
<td></td>
</tr>
</tbody>
</table>

## Key

- **Routine schedule MenC**
- **Routine schedule ACWY**
- **School based catch-up ACWY**
- **Primary care catch-up cohorts**
Cumulative totals of lab confirmed MenW disease, England
Age distribution of MenW cases by epidemiological year (July- Jan only)
Decision to Stop 3 month MenC dose

- MenC disease is extremely rare in the UK.
- Most children currently rely on herd protection due to rapid waning of immunity in infants and toddlers.
- Recent studies show that a MenC to MenACWY programme is likely to maintain high levels of herd protection.
- Only 0-2 cases annually in infants (<1 year-olds).
- Currently 800,000 doses of MCC at 3 months of age.
- Gaps for additional vaccines at 3m [? PCV13].

PHE REPORT TO JCVI

Removing the 3-month MenC dose may lead to 4 additional cases in infants and 1 additional case in toddlers annually.
Overall, cases of IMD in <1 years of age have fallen since the MenB programme was introduced.

There were 119 cases in 2014/15 compared to only 90 in 2017/18 (July to May inclusive).

This reduction has been driven by the impact of MenB vaccination, as MenB case numbers in infants fell by 39 (42% fall).

Over the same time period, MenW and MenY cases in infants have remained fairly stable over the last 4 years.

In contrast, MenC infant cases have increased from 1 to 12.
MenC cases < 1 year, England

- 7/12 (58.3%) occurred in one region 10.9 per 100,000

- The two recent MenC infant deaths & one known severe infant case with life-changing outcomes were also reported from this region.

- As there have been no epidemiological links identified between the infant cases, this would suggest increased circulation of MenC within the community of that region.

- The adolescent MenCAWY programme is expected to control circulation of MenC by reducing rates of carriage in young adults.

- As no substantial difference in the meningococcal immunisation programmes, vaccine coverage rates or performance in the region suggests that the excess cases are a very unfortunate but random event.
MenB cases continue to decline from 349 in 2015/6 to 277 in 2016/17.
4CMenB continues to have a significant impact on MenB disease in infants and toddlers.
Surveillance on-going … > 3 million doses … No safety concerns so far.
MenW cases across all age groups have declined for the first time in 2017/18.
In infants, there is some evidence of 4CMenB impact on MenW disease, but very few cases.
Cases of serogroup C are being closely monitored.
Acknowledgements

PHE MRU Manchester:


PHE Colindale:

Sydel R. Parikh, Nick J. Andrews, Kazim Beebeejaun, Helen Campbell, Sonia Ribeiro, Mary E. Ramsay, Shamez N. Ladhani, Vanessa Saliba, Sema Mandal

MRF MENINGOCOCCUS GENOME LIBRARY
(http://www.meningitis.org/research/genome).