Invasive Meningococcal Disease
- prevention through vaccination

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“a pain you cannot describe”
Two weeks of Hell
Petition

Give the Meningitis B vaccine to ALL children, not just newborn babies.

All children are at risk from this terrible infection, yet the Government plan to only vaccinate 2-5 month olds. There needs to be a rollout programme to vaccinate all children, at least up to age 11. Meningococcal infections can be very serious, causing MENINGITIS, SEPTICAEMIA & DEATH.

More details

Sign this petition

816,118 signatures

Show on a map 100,000
Vaccines against MenB

• MenC and MenACWY conjugate vaccines target the polysaccharide capsules – no cross-protection

• MenB polysaccharide is a polysialic acid - identical to that found on surface of human foetal neuronal cells.

• Consequently;
  (i) Poorly immunogenic.
  (ii) Potential to induce an autoimmune response

• Use subcapsular antigens, which:
  (i) are Surface-exposed
  (ii) are Conserved
  (iii) induce Bactericidal activity
BEXSERO® Consists of 4 Antigenic Components Chosen to Achieve Broad Protection

- **fHbp**: factor H binding protein
  - Binds factor H, which enables bacterial survival in the blood\(^1,2\)

- **NadA**: neisserial adhesin A
  - Promotes adherence to and invasion of human epithelial cells\(^3-5\)
  - May be important for colonisation\(^4\)

- **NHBA**: neisseria heparin-binding antigen
  - Binds heparin, which may promote bacterial survival in the blood\(^7\)
  - Present in virtually all strains\(^6,7\)

- **NZ PorA P1.4**: porin A
  - Major outer membrane vesicle protein—induces strain-specific bactericidal response\(^8\)

Combining antigens that target different steps of meningococcal pathogenesis is likely to help optimize MenB vaccine effectiveness

Predicted meningococcal strain coverage in Europe

*Figure 1: Percentages of isolates predicted by the meningococcal antigen typing system to be covered, and number of antigens, overall and by country*
Invasive Meningococcal Disease
England & Wales, 2008-14
Laboratory confirmed cases
invasive meningococcal disease
England and Wales
Laboratory confirmed cases of invasive meningococcal disease capsular group B (MenB) in England, calendar years 2009-2014

Date source: PHE Meningococcal Reference Unit. Surveillance by PHE Immunisation Department – Last Update August 2015
Please see link for more information and data https://www.gov.uk/government/collections/meningococcal-disease-guidance-data-and-analysis
Long term trends in notified meningococcal disease, England and Wales
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)
Laboratory confirmed IMD by group and age (2010-2014)
MenB cases/deaths, England 2014/15

![Bar chart showing the number of cases and deaths by age in years for MenB in England 2014/15. The chart indicates a peak in cases and deaths in the 0-1 year age group, with a significant decrease in cases and deaths in older age groups.](image)
IMD in <2 year-olds
England & Wales (2006/07-2010/11)
Proportion of children with bactericidal antibody (GMT) to specific strains at different schedules

<table>
<thead>
<tr>
<th>Study</th>
<th>Schedule</th>
<th>44/76 fHBP</th>
<th>5/99 NadA</th>
<th>NZ 98/254 OMV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Findlow (≥1:4 hSBA)</td>
<td>2, 4, 6 m After third dose</td>
<td>95% (30)</td>
<td>95% (126)</td>
<td>85% (19)</td>
</tr>
<tr>
<td></td>
<td>2, 4 m After second dose</td>
<td>87% (28)</td>
<td>100% (104)</td>
<td>74% (6.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gossger (≥1:5 hSBA)</td>
<td>2, 3, 4 m</td>
<td>99.3% (82)</td>
<td>100% (323)</td>
<td>81% (11)</td>
</tr>
</tbody>
</table>
Adverse reactions to 4CMenB

Bexsero® is associated with higher rates of local and systemic reactions when given with other routine infant vaccinations

- similar to those seen with whole cell pertussis vaccines

Systemic effects tend to be additive when given with other vaccines

For example, any fever was seen following:

- 26-41% of Bexsero® doses when administered alone,
- 23-36% after routine vaccines given alone
- 51-61% after Bexsero® and routine vaccines administered together
*No increase in the incidence or severity of the adverse reactions was seen with subsequent doses of the vaccination series.

†Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib; BEXSERO+Routine: N=2478; MenC+Routine: N=490; Routine: N=659.

‡Fever was categorized as severe if temperature was ≥40°C. All other reactions were categorized as severe if subject was unable to perform normal daily activities.

When Fever Occurred, it Generally Followed a Predictable Pattern, With the Majority Resolving the Day After Vaccination. *BEXSERO® given with routine vaccines—post–dose 1*

**Post–dose 1**
*(2-4-6 month dosing schedule)*

![Graph showing fever patterns](image)

*Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib; BEXSERO+Routine: N=2433–2478; MenC+Routine: N=486–490; Routine only: N=643–659.*

Fever was defined as rectal temperature ≥38.5°C.

In general, the frequency of medically attended fever was low

Percentage of Subjects With Medically Attended Fever
(Number of Subjects With Medically Attended Fever/Total Number of Subjects)

<table>
<thead>
<tr>
<th>Subset</th>
<th>BEXSERO® Vaccine</th>
<th>MenC+ Routine Vaccines*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observer-Blind Subset Any dose</td>
<td>5.3% (26/493)</td>
<td>2.8% (13/470)</td>
</tr>
<tr>
<td>Open-Label Subset Any dose</td>
<td>1.4% (28/1966)</td>
<td>1.8% (12/659)</td>
</tr>
</tbody>
</table>

*Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib.

Use of antipyretic agents

Effect of prophylactic paracetamol administration at time of vaccination on febrile reactions and antibody responses in children: two open-label, randomised controlled trials

Roman Prymula, Claire-Anne Siegrist, Roman Chlibek, Helena Zemlickova, Marie Vackova, Jan Smetana, Patricia Lommel, Eva Kaliskova, Dorota Borys, Lode Schuerman

In 2010, JCVI recommended that paracetamol should not be routinely offered to infants to prevent fever because it may interfere with vaccine responses.
Prophylactic Paracetamol at the Time of and Closely After Vaccination Reduced Fever
When BEXSERO® is given concomitantly with routine infant vaccines

NPP: no prophylactic paracetamol (N=182); PP: with prophylactic paracetamol (N=178-179).
Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib.

Prophylactic Paracetamol at the Time of and Closely After Vaccination Did Not Impact Immunogenicity of BEXSERO®

BEXSERO given concomitantly with routine infant vaccines 2-3-4 month schedule

<table>
<thead>
<tr>
<th></th>
<th>BEXSERO+routine at baseline*</th>
<th>BEXSERO+routine+paracetamol at baseline†</th>
<th>BEXSERO+routine at 1 month post–final dose*</th>
<th>BEXSERO+routine+paracetamol at 1 month post–final dose†</th>
</tr>
</thead>
<tbody>
<tr>
<td>fHbp</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>NadA</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>PorA P1.4</td>
<td>78</td>
<td>74</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NHBA</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
</tbody>
</table>

* N=165–171; † N=160–169.
Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib.
NT=not tested.

1. Prymula R, et al. Presented at: 29th Annual Meeting of the European Society for Paediatric Infectious Disease (ESPID); 7-10 June 2011; The Hague, The Netherlands; Poster #631; 2. BEXSERO [summary of product characteristics].
Siena, Italy: Novartis Vaccines and Diagnostics S.r.l.; January 14, 2013.
Systematic review in 2014
The effect of prophylactic antipyretic administration on adverse reactions and antibody response in children

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Paracetamol</th>
<th>No paracetamol</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hayat 2011</td>
<td>23</td>
<td>118</td>
<td>0.18 [0.10, 0.32]</td>
</tr>
<tr>
<td>Ipp 1987</td>
<td>62</td>
<td>233</td>
<td>0.47 [0.32, 0.70]</td>
</tr>
<tr>
<td>Jackson 2011</td>
<td>25</td>
<td>176</td>
<td>0.58 [0.33, 1.01]</td>
</tr>
<tr>
<td>Lewis 1988</td>
<td>35</td>
<td>115</td>
<td>0.38 [0.22, 0.66]</td>
</tr>
<tr>
<td>Prymula 2009</td>
<td>94</td>
<td>226</td>
<td>0.37 [0.25, 0.53]</td>
</tr>
<tr>
<td>Rose 2013</td>
<td>43</td>
<td>100</td>
<td>0.25 [0.14, 0.43]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>968</td>
<td>976</td>
<td>0.35 [0.26, 0.48]</td>
</tr>
</tbody>
</table>

Also reduction in
- Pain, swelling and redness at injection site
- Irritability, drowsiness, persistent crying and loss of appetite
- Although reduction in antibody was observed, size of reduction was considered unlikely to result in clinically significant reduction in protection

Das RR et al PLoS ONE 9(9): e106629. doi:10.1371/journal.pone.0106629
### Timing of paracetamol doses with other infant vaccines

<table>
<thead>
<tr>
<th></th>
<th>PCV13 + Infanrix Hexa + Paracetamol Twice Daily</th>
<th>PCV13 + Infanrix Hexa + Ibuprofen Twice Daily</th>
<th>PCV13 + Infanrix Hexa + Paracetamol Thrice Daily</th>
<th>PCV13 + Infanrix Hexa + Ibuprofen Thrice Daily</th>
<th>PCV13 + Infanrix Hexa</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Participants</strong></td>
<td>149</td>
<td>157</td>
<td>147</td>
<td>155</td>
<td>187</td>
</tr>
<tr>
<td><strong>Percentage of Participants Reporting Fever Within 4 Days:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever ≥38 - ≤39 °C</td>
<td>32.9</td>
<td>45.2</td>
<td>18.4</td>
<td>34.2</td>
<td><strong>41.7</strong></td>
</tr>
<tr>
<td>Fever &gt;39, ≤40 °C</td>
<td>1.4</td>
<td>1.4</td>
<td>0.7</td>
<td>0.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Fever &gt;40 °C</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Clinical Trials.gov:** Study Assessing the Effect of Medications to Prevent Fever on Prevenar 13®

Summary of evidence on paracetamol

- Fever is common after Bexsero® and fever rates are additive to those normally seen after infant vaccines
- Concern about high rate of medical attendance
- Fever peaks at six hours after vaccine, uncommon after 48 hours
- Rates and intensity of fever reduced by prophylactic paracetamol
- Immunogenicity of concomitant infant vaccines not reduced when given with paracetamol and Bexsero®

- Studies with other infant vaccines show
- Paracetamol also reduces other systemic and local reactions
- three doses of paracetamol starting immediately is better than two doses starting at 6 hours (suggests first dose is the most important)
- Paracetamol superior to ibuprofen in preventing fever and symptoms
How has it gone?

Vaccine eligibility

- Children getting MenB “booster” at 12-13 months of age in absence of primary course
- Children born after 1st May who had already completed their primary course
  - Eligible under contract but not being actively called
- Confusion between catch-up cohorts and those in eligible cohort who present late (e.g. movements from abroad)
- Requests for children who had started private vaccinations
- Very few calls after first few weeks
How has it gone?

Use of paracetamol

• Nurses wanting to administer during vaccination clinic
• Parents taking before come in to see the nurse
• How long to wait (could they wait to get cheaper product in local supermarket)
• Pharmacists refusing to sell because outside product license
• Premature and small for dates babies
  • Need individual prescription
  • Neonatal units refusing to give paracetamol
• Very few calls after first few weeks
Conclusions

1. The UK is the first country to introduce routine MenB vaccine

2. Post marketing surveillance will be essential to provide international experience for other to build on

3. MenB implementation in the UK is built on successful infant programme in general practice

4. The vaccine should protect against 73-88% of MenB cases in vaccinated infants and toddlers

5. Recommending paracetamol prophylaxis has been challenging but, so far, successful

6. The programme is supported by range of communication materials

7. No significant concerns in the first 6 months of the programme
Collection

Immunisation

Organisation: Public Health England
Page history: Updated 23 January 2014, see all updates

Immunisation information for health professionals and immunisation practitioners.

Contents
- Documents

Immunisation is the most important way of protecting individuals and the community from vaccine preventable infectious diseases.

‘Immunisation against infectious disease’, also known as the Green Book, has
Resources for health professionals and patients

- PHE MenB Health Care Worker Q+A
- PHE MenB vaccine leaflet (long version)
- PHE MenB vaccine leaflet: 3 minute guide
- PHE MenACWY vaccination programme patient information leaflet and posters
- PHE MenACWY Health Care Worker Q+A
- PHE Paracetamol Patient Information Leaflet
- Training the trainer slide sets and animated voice over
- OVG video on parent consultation

- Meningitis Research Foundation:  http://www.meningitis.org/
- Meningitis Now.  https://www.meningitisnow.org/
Public Health England

Protecting your baby against meningitis and septicaemia caused by meningococcal B bacteria

MenB vaccine now available!

Protecting your baby against meningitis and septicaemia caused by meningococcal B bacteria

MenB vaccine now available!
Information about the MenB vaccine and recommended paracetamol use

Immunisation
The safest way to protect the health of your baby