Preventing meningitis in teenagers vaccinated against MenB as babies: is one booster dose enough?

Progress report for The Jessica Bethell Foundation: we are very grateful to The Jessica Bethell Foundation for their support, and are pleased to report the year one research findings.

Background

Currently, in the UK only babies are vaccinated against Meningococcal group B disease (MenB), as they are the age group at the highest risk of disease.

However, beyond the age of five, teenagers and young adults are the next most at risk of developing disease. One reason for not introducing a teenage vaccination programme was cost, particularly since current evidence suggests that teenagers would need two doses of MenB vaccine to be protected.

However, in the future, most teenagers will have been routinely vaccinated as babies. Therefore, it is possible that these teenagers may only need one dose of the vaccine to extend their protection through this next 'at risk' period. This would greatly reduce the cost of a teenage MenB programme and provide the opportunity to re-evaluate its cost-effectiveness.

The babies involved in the first clinical trials of the MenB vaccine which were carried out at Oxford, are now approaching adolescence – offering a unique opportunity to obtain the first ever data on whether a booster dose of the vaccine given in the second decade of life, can protect teenagers and young adults against MenB disease.

Study objectives

This study is a collaboration being led by Professor Andrew Pollard, Director of Oxford Vaccine Group, and Prof Ray Borrow, Head of the Vaccine Evaluation Unit at Public Health England, Manchester, and aims to find out:

- Whether children approaching adolescence retain any protection against MenB from their infant vaccines
- Whether a single dose of the MenB vaccine is enough to boost immunity gained from infant vaccination

Progress

In the first year of the project, the research team successfully gained all of the necessary ethical approvals and achieved their recruitment targets; enrolling 70 children to participate in the research.

The children have been divided into four different study groups, two of which are 'intervention groups', (involving 40 children) and two of which are 'control groups' (involving 30 children). For the intervention group, the group a child was allocated to depended on which MenB vaccine schedule they received in the original clinical trials. For the control group, children were randomly allocated to one of the two groups.

To enrol all 40 children to the intervention group, the team had to overcome many challenges, given that it has been over ten years since the original vaccine trials took place, therefore many families were no longer contactable using their last known contact details. To overcome such challenges, the researchers made contact with GP surgeries and Thames Valley Child Health Information Services (CHIS). The additional 30 children recruited, are 'age matched controls', i.e. they are children of the same age as those in the 'intervention groups', but they have never been vaccinated against MenB. These children are therefore referred to in the research as being 'naïve' participants. The control group children were principally recruited through mail outs sent out in the Oxfordshire area.

All of the children recruited will take part in four different study visits, conducted over a year. The procedures that take place at each visit differ depending on which group the child is allocated to (as shown in Table 1), however all children will have four blood tests performed, over the course of the year. All visits and study procedures take place at the child's home, or within a central location such as a hospital outpatients clinic.

For all children, the first study visit involved a blood sample being taken, before the MenB vaccine was given. This will enable the research team to see if children in the intervention group still have an immune response present after being vaccinated as an infant. Samples collected form the control groups will provide a comparison.

Blood samples collected at visits 2, 3 and 4 are taken after all children have received one dose of MenB vaccine in this study. This will allow the research team to compare the immune response between one dose of the MenB vaccine in those vaccinated as an infant or toddler and those who were not. As the study hypothesis is that one dose of the vaccine may produce a stronger response in pre-vaccinated children.

	Visit 1 (Day 0)	**Visit 2 (Day 28)**	**Visit 3 (Day 180)**	**Visit 4 (Day 365)**
Group 1 (Intervention)	Blood sample + Vaccine	Blood sample	Blood sample	Blood sample
Group 2 (Intervention)	Blood sample + Vaccine	Blood sample	Blood sample	Blood sample
Group 3 (Control)	Blood sample + Vaccine	Blood sample	Blood sample	Blood sample + Vaccine
Group 4 (Control)	Blood sample + Vaccine	Blood sample + Vaccine	Blood sample	Blood sample

Table 1: Summarises what happens during the research study

The team have made excellent progress with the study visits. In the 'intervention group', all 40 children have completed visit 1, 38 have completed visit 2 and 35 have completed visit three. For the control group children, all 30 children have completed visit 1, 29 have completed visit 2, and 2 children have completed visit 3.

Next steps

The research team are now focusing on completing all four study visits, and are currently in the process of booking in the remaining visits with the study participants.

After all participants have completed their third study visits, blood samples will be sent to Public Health England, Manchester, where they will be analysed at Professor Ray Borrow's lab. Here, the levels of antibodies will be measured in the blood, using specialised laboratory tests. The results of these tests will enable the researchers to understand from the level of antibody in the blood, whether a child is protected against MenB or not.

This will yield important information regarding the immune responses in several different groups of children to different schedules of MenB vaccine. The study will ultimately inform decisions about whether or not to include an adolescent booster meningococcal B vaccine into the UK routine immunisation schedule.

A year's follow up is required for all children participating in the study, meaning that the study is currently anticipated to finish in January 2020.