Public Health England

Baby vaccine study (Sched3)

Full title: Assessment of post booster antibody responses in UK infants given a reduced priming schedule of meningococcal serogroup B and 13 valent pneumococcal conjugate vaccines

Public Health England and Oxford Vaccine Group, part of the University of Oxford are conducting a study on behalf of the Department of Health assessing new vaccination schedules, which would include all the routine vaccines, only in a different way. You have been contacted because you have a baby who will shortly be invited for their first vaccinations.

Vaccines activate the immune system to make antibodies, which move round the body in the blood and protect against infections. We will measure the levels of antibody to the vaccines given to babies and will offer extra dose(s) of the Hib, meningitis B, meningitis C and pneumococcal vaccines if there are not enough antibodies for protection. We would like to invite your family to take part in this study.

The study will involve 200 babies. Before you decide if you would like your baby to join this study, you need to understand the reasons why it is being done and what it would involve. Please take the time to read the following information carefully and talk to others about the study if you wish, including asking your study nurse any questions you have.

What is the purpose of the study?

The Department of Health have made a recent change to the routine immunisation programme for babies with the introduction of a meningitis B vaccine, called Bexsero. This study will provide information about how best to include it by assessing two different vaccine schedules by measuring antibodies your baby has to the vaccinations. This will be important both for you to be reassured they have protection against this deadly infection, as well as helping the Department of Health continue to ensure the best protection is offered to our population. To do this children in the study will receive:

- A dose of the MenB vaccine at 2, 4 and 12 months of age (as recently introduced to the routine immunisation schedule)
- A vaccine against Meningitis C (MenC) disease at 12 months of age, instead of at 3 and 12 months of age as currently given in the routine schedule.
- The 13-valent pneumococcal vaccine (PCV13) either at 2, 4 and 12 months of age (as currently given in the routine schedule) or at 3 and 12 months of age.

Rates of disease prevented by PCV13 and MenC vaccines are now low in the UK and babies are protected by herd immunity (protection received by others in the community being vaccinated). It is therefore not expected that babies taking part in this study will be at an increased risk from these diseases whichever vaccine schedule they receive. In particular the reduction in MenC vaccine doses is in line with a change recently recommended by the JCVI (the group that advises the Department of Health on vaccination), who felt that this should still provide adequate protection for babies. If your baby has low antibody levels, we will offer extra dose(s) of the appropriate vaccine(s).

It would be important for us to know if the babies Mum had a whooping cough vaccine during pregnancy, and when that happened, so we would ask your permission to check the dates with your GP.

Why is my baby being invited to take part?

We are inviting all babies due their first vaccinations who are registered with participating GP surgeries in Hertfordshire and Gloucestershire.

Does my baby have to take part?

No, it is up to you to decide whether you would like them to take part. If you agree, you will be asked to sign a consent form. Participation is entirely voluntary and you can withdraw them from the study at any time without giving a reason and this would not affect your babies routine care. If you do not wish to participate or if you withdraw during the study, you will be offered your babies routine immunisations through the GP surgery. If a blood sample has already been taken, you will need to decide if you want the sample to be destroyed, in which case you will need to inform us in writing. If the sample has already been tested, we will send you and your GP the results with any further dose recommendations.

What will happen to my baby if they take part?

The timing of the vaccinations and blood tests are shown in the table below. The first appointment should last around an hour and all following appointments about 30 minutes.

If you agree your baby can take part, a member of the study team will arrange an appointment to meet you at your convenience to answer any further questions that you may have, check their health and complete the consent form.

To decide which vaccine schedule your baby receives, they would be randomly assigned a group. This is chosen by a computer programme and allocation is by chance, like tossing

a coin. You or the study team would not be able to influence which group your child was assigned to. There is a 50% chance of your baby being in either group.
The study team will give your baby all of the vaccinations and will take the blood samples and nose swabs. The amount of blood collected from your baby will be about one teaspoon. If the study team is unable to obtain a blood sample from your baby, you will be given the option to re-schedule the appointment or miss that sample.

This study involves two blood samples so we can measure their antibody levels: after their baby vaccines, at about 5 months of age, and after their booster vaccines, at about 13 months of age. In order to reduce any discomfort, the nurse will offer you some local anaesthetic cream or cold spray to numb the skin for your baby before taking the blood sample. Some of the germs we vaccinate against are carried in people's noses. We would like to take a swab of your child's nose just before the booster vaccines at a year of age and six months later.

We will let your GP know that your baby is taking part in the study and will write to you and your GP with the results of the blood tests. If your baby does not develop enough antibodies against the Men B, MenC, Hib or pneumococcal vaccines, the study team will contact you to offer your baby an extra dose of vaccine(s).

This is the schedule of what happens each time you see your nurse:

<table>
<tr><th>Group</th><th>Visit 1
2 months of age</th><th>Visit 2
3 months of age</th><th>Visit 3
4 months of age</th><th>Visit 4
5 months of age</th><th>Visit 5
12 months of age</th><th>Visit 6
13 months of age</th><th>Visit 7
18 months of age</th></tr>
<tr><td>1 (n=100)</td><td>Infanrix
Bexsero
PCV13
Rota</td><td>Infanrix
Rota</td><td>Infanrix
Bexsero
PCV13</td><td rowspan="2">Blood sample</td><td rowspan="2">Menitorix
Bexsero
PCV13
Nose swab</td><td rowspan="2">MMR
Blood sample</td><td rowspan="2">Nose swab</td></tr>
<tr><td>2 (n=100)</td><td>Infanrix
Bexsero
Rota</td><td>Infanrix
PCV13
Rota</td><td>Infanrix
Bexsero</td></tr>
</table>

Infanrix (Infanrix-IPV-Hib) = Diptheria-tetanus-whooping cough (pertussis)-polio-Hib

Bexsero = Meningitis B

PCV13 (Prevenar13) = Pneumococcal Disease

Rotarix = Rota, Rotavirus – this vaccine is given as drops into the mouth that the baby swallows.

Menitorix = Meningitis C /Hib

MMR = Measles, Mumps, Rubella

To decide which vaccine schedule your baby receives, they would be randomly assigned a group. This is chosen by a computer programme and allocation is by chance, like tossing a coin. You or the study team would not be able to influence which group your child was assigned to. There is a 50% chance of your baby being in either group.

What are the alternatives?

If you do not wish to take part in this study, then you do not need to do anything

Taking part in this research study is completely voluntary and if you decide to say no, it will not affect your child's routine care in any way. If you do not take part in this study your child will still be able to have their routine immunisations at your GP surgery. Your GP surgery will contact you for your babies routine vaccinations at the appropriate times

You are also free to change your mind and withdraw your child at any time without giving an explanation, in which case your child's GP would provide the remaining routine vaccinations. If you did withdraw your child from the study and a blood sample has already been taken, you will need to decide if you want the sample to be destroyed, in which case you will need to inform us in writing. If the sample has already been tested, we will send you and your GP the results with any further dose recommendations.

What are the possible disadvantages and risks as well as benefits of taking part?

Your baby will have the advantage of being offered an extra dose of vaccine if antibodies against Hib, Men B, MenC or pneumococcal are found to be low. We will also provide the routine vaccines at a time that is convenient for you. This study will involve two blood tests and the nose swab that are not part of routine care.

There is also a benefit to the community, as our results will be used to inform future vaccination policy by the Department of Health.

What are the side-effects when taking part?

The blood test may be uncomfortable but will be performed by experienced nurses or doctors, and creams or sprays will be offered to minimise discomfort. As with all vaccines, there may be some redness and mild swelling where the injection is given and some babies sleeping and eating patterns may change for a few days. We do not anticipate any other side-effects.

As with all vaccines, there is a small chance of an allergic reaction to the vaccine, so we would monitor your child for 20minutes following each injection. The study nurses/doctors are specifically trained and equipped to deal with this unlikely event.

The Department of Health is recommending that any babies given meningitis B vaccine, which can cause fever, are given three doses of infant paracetamol in the 24 hours after vaccination. We will give you some baby paracetamol and your nurse will explain how to use it and how to record this in the health diary. The nose swab may be a little uncomfortable and make the eyes water for a couple of minutes.

What happens when the study stops?

We will write to you with the results of your babies blood tests. If your baby does not have enough antibodies against the Men B, MenC, Hib or pneumococcal vaccines, the study team will contact you to offer your baby an extra dose of vaccine(s). When the study finishes, your baby will continue to be looked after by their GP.

In summary:

Babies will receive their routine vaccinations including the MenB vaccination, with a differing number of doses of the MenC and pneumococcal vaccines

The study involves two blood samples from babies to check the amount of antibody made in response to vaccinations given. If the blood test shows low antibody levels against Men B, MenC, Hib or pneumococcal vaccines, the study team will contact you to recommend an extra dose of vaccine(s) for your baby.

What if relevant new information becomes available?

Sometimes we get new information about vaccines or vaccination schedules that might be relevant to this study. If that happens or if the study is stopped for any reason, we will write to you and your GP with information about you and your babies continuing care.

What if there is a problem?

- **Complaints**

  If you have concerns about any aspect of this study, you can contact the study Principal Investigator (contact details below), who will do their best to answer your questions. If you remain unhappy and wish to complain formally, then you can do this through the NHS Complaints Procedure, details of which can be obtained at www.nhs.uk or by phoning 0845 601 3012 or you may contact the study sponsor; University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572224, or the head of CTRG, email ctrg@admin.ox.ac.uk

- **Harm**

  We do not anticipate any harm resulting from obtaining blood samples. All vaccines used in this study are licensed and covered by the Manufacturers' product liability The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. The National Health Service complaints mechanism will still be available to you.

Will our participation in the study be kept confidential?

Personal data may include name and address of your baby as well as the blood test results and relevant medical information that would allow us to analyse the results and answer the study objectives. The only people with access to this information will be employees of the PHE, Department of Health or regulatory authorities who may wish to check the study is being carried out within the appropriate guidelines. The data will only

be used for the purposes of this study, will be stored in secure PHE facilities and will be destroyed after an appropriate time period, which may be a number of years.
To check that the study was being conducted correctly, your child's study records might be read (but not kept) by representatives of the following groups without violating your child's confidentiality:

- UK Medicines and Healthcare products Regulatory Agency (MHRA)
- The NHS trusts that have given approval for this study
- Responsible members of the University of Oxford may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations.

Involvement of my babies GP

With your permission, we will send a letter to your babies GP to let them know that they are taking part in the study. We will also inform your babies GP of their blood results and all vaccinations so that they can be added to your babies medical records.

What will happen to any samples from my baby?

The blood samples we take for this study will be labelled with a study number and tested anonymously in certified laboratories. We will write to you and your GP with the results of the antibody levels and, if needed, recommendations for further vaccination(s). Once the tests are complete, there may be small amounts of blood remaining from your baby. We would like your permission to use any blood remaining after these tests to help us better understand why some babies develop infections and how vaccines work to protect them. You will be asked to consent for this separately in the consent form. If you are not happy for the left over blood sample to be used for any other tests, please cross out the relevant section in the consent form and the samples will be destroyed after antibody testing. Your decision regarding the leftover blood will not affect your babies participation in the study.

What will happen to the results of the research study?

We plan to publish the results in a medical journal that will be accessible to the public. The results of the study will also be reported to the Department of Health to help planning national vaccination programmes in the future. None of the reports will contain any information that might allow the readers to identify any babies who took part in the study. At the end of the study, we will also write to all participating families to summarise the overall findings.

Who is sponsoring and funding the research?

The study is funded by the UK Department of Health and Bill and Melinda Gates Foundation, and is being sponsored by University of Oxford. PHE (Public Health England) and Oxford Vaccine Group are running the study, PHE is part of the Department of Health and has the remit of protecting the health and well-being of the population.

Who reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect the safety, rights, well-being and dignity of individuals. This study has been reviewed and given favourable opinion by the South Central Berkshire Research Ethics Committee (Ref: 15/SC/0355). Details of this study can be found on the following website: www.ClinicalTrials.gov (Ref: NCT02482636).

Further information and contact details.
If you have any questions, you can ask your study team or contact Professor Elizabeth Miller on 020 8327 7430 or Dr Jo Southern on 0208 327 6084.

We do hope that you and your family will take part in this study. Your contribution could be an important step towards the continual improvement of vaccine policy in the UK.

You and your child(ren) may be invited to take part in future studies with us by virtue of the GP surgery that you attend. We reassure you that invitation for future studies will not be related to individual results we obtain from this study.

Sticker with VRN name and contact details (depending on site)