

Gambian Pertussis Study- GaPs

Informed Consent Document

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Study Title: GaPs

SCC Number: 1600v3 **Sponsor:** MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine

What is informed consent?

You are invited to take part in a research study. Participating in a research study is not the same as getting normal care during pregnancy or normal care for your newborn baby. Normal care aims to ensure that you and your baby remain healthy. The purpose of this research is to try to find new ways to keep all babies healthy in your community, across The Gambia and in other parts of the world in the future. It is your choice whether you want to take part or not. You should not feel any obligation.

Before you decide you need to understand all the information about the study, why we are doing it and what it will involve. Please take time to read the information or get the information explained to you in your language. Listen carefully and feel free to ask if there is anything that you do not understand. We will ask you some questions to check that we have explained everything properly too. As the study will also involve your new baby it is very important that you also discuss it with your spouse - the father of your baby - and that he agrees that it is OK to take part too. You may also want to ask other members of your family. If you decide to join the study, you will need to sign or thumbprint a consent form saying you understand and agree to be in the study. You will receive a copy of the form.

Why is this study being done?

One important cause of serious infections in the first few months of life is a germ called *Bordetella pertussis*. This germ causes a disease called whooping cough which can be very serious for young babies and leads to difficulties in breathing and a long-lasting cough. Whooping cough kills many children, including newborn babies across the world and finding new ways to protect newborns in the first few months of life is therefore very important.

A vaccine against whooping cough (the pertussis vaccine) is already given to babies across the world, including in The Gambia, when they are given around 2, 3 and 4 months of age. This is recommended by the World Health Organisation. The vaccine is good at protecting babies and children from the disease. However, because the vaccine is only given at 2, 3 and 4 months of age, babies are often not fully protected against this infection until they are 4 or 5 months old. This leaves them at high risk of serious disease caused by whooping cough in the first few months of life. There are also two types of whooping cough vaccines- one called whole cell, which is the one already used in The Gambia, and one called acellular, which is mainly used in Europe and North America. The names just relate to how the vaccine is made. At the moment it is a bit unclear which one is the better one to use for children worldwide and our study wants to provide scientific evidence for making these decisions. One aim of this study is to find new ways to protect newborn babies against the whooping cough germ from the time of birth and in the first few months of life. One way to do that is to give the vaccine to the women during pregnancy, like we already do to prevent tetanus in The Gambia. The other aim is to find out which of the two available vaccine types might work better for children in the long term. And finally we need to check that giving the vaccines to the mothers in pregnancy does not cause any interferences with the vaccines given to the baby later.

What vaccines will be involved?

The vaccine being used in the study (which is called Boostrix-IPV) is exactly the same vaccine that is already given to many pregnant women across many parts of the world where there has been a big problem with whooping cough in babies, like in the UK. It also protects against tetanus and diphtheria and polio. It has not yet been used routinely for women in The Gambia, but is expected to work just the same as it does in the other countries, and there are a lot of data on its safety already. The vaccines to be used for the babies have been given to millions of children worldwide already and we know that they are safe and effective in this age group.

In this study, we want to find out two main things:

Firstly, we want to see if giving a dose of the Boostrix-IPV vaccine to Gambian women while they are pregnant will allow them to pass on protection (immunity) to their baby before they are born. This might work in the same way that you pass energy and nutrients to your unborn baby to help it grow inside you and could mean

your baby is protected from birth. One group of pregnant women will get the Boostrix-IPV vaccine, whilst the other group gets the routinely recommended tetanus injection. This will also allow us to study any effect of vaccinating the women in pregnancy on the vaccines subsequently given to their babies and how long the immunity lasts in the women.

Secondly, all babies will get a whooping cough vaccine at 2, 3 and 4 months of age, but they will be divided into two groups to compare the two different vaccines currently available to check if there is a difference in the immunity they induce. They will also be allocated to further subgroups to come back on different days to have another blood sample taken. In some babies, we will also collect samples from the nose at the same visit. This is because we have recently learned more about the important role that the lining of the inside of the nose, known as the 'mucosa', might play in protecting us against pertussis bacteria. Analysing your baby's mucosal samples, in addition to their blood samples, will help us to better understand the differences between the two whooping cough vaccines and to design improved vaccines in the future. We want to study many time points to understand where and how the immunity is built up, but we are also mindful that we cannot take too many repeated samples from the same baby, hence they have to be in a number of different groups. The total time your baby would be giving a small amount of blood over the first 9 months of life will be a maximum of 5 times and the volumes will be no more than a tablespoon. Nasal samples will only need to be collected from some of the baby groups and this will happen at the same time points as the blood samples, therefore, not requiring any extra visits. All other EPI vaccines your baby should receive will be given by the study team as per usual schedule.

If you decide to take part in the study and are eligible, you and your baby will get the whooping cough vaccines according to allocated groups. The group that you and your baby are in is picked by chance. You cannot decide and we cannot decide either.

What does this study involve?

We wish to recruit 600 pregnant women to the study and we will continue to monitor their newborn babies until they reach 9 months of age. It is very important that you are planning to deliver in Sukuta or Faji Kunda health centre rather than at home and also that you do not plan to travel away from the coastal area if you want to take part. If you plan to deliver elsewhere or plan to travel when your baby is less than 9 months of age it is very important that you let us know now.

Screening visits

If you agree and sign the consent form, we will assess you to see if you are eligible and also to check that it is likely to be safe for you to take part. Study staff will talk to you about any previous pregnancies, about your general health and about any medications you are taking. If you remain eligible, you will have a picture (an ultrasound scan) of your baby taken at either the health centre or at the MRC in Fajara. This is to tell us when we think your baby will be born. We will tell you this too and you can also see the picture. The scan is safe and does not cause any pain. A blood sample of 5mL (1 teaspoon) will be taken from you. The sample will be tested for HIV, hepatitis B and syphilis infections. We will discuss the meaning of these tests with and you can decide if you agree to them. If you decide you don't want the tests or if we find you have one of these infections you will not be able to take part in the study. A test for sickle cell disease, for anaemia and for blood group, will also be taken. Any of these tests, or other tests, could be repeated during screening to ensure there are no problems. We will explain if additional tests are needed and confirm whether or not you agree to them.

Randomization and vaccination

You will be invited back to the health centre 2 to 3 months before your baby is due. We will discuss your health, the current pregnancy and medications and the doctor will examine you.

If we discover you are sick, are carrying twins or if you have problems with the current or past pregnancies you will not be able to participate in the study. You will receive immediate care at the study site and then be referred to the appropriate health care facility in The Gambia. We will explain the reasons for this to you.

If you are found to be eligible to participate, we will check that you are well on the day, that there are no concerns about your pregnancy and we will take a 5mL (1 teaspoon) blood sample to test for the protection you have against whooping cough and tetanus, and to test for malaria. We will save a bit of your blood for future tests for markers of infections and vaccine responses (2-3 ml). You will then be picked by chance ('randomized') to join one of the two pregnancy vaccine groups. Either you receive a whooping cough vaccine in pregnancy or you receive the tetanus vaccine. Neither you nor most of the study team will know if you get the whooping cough or tetanus vaccine injection in pregnancy. This is called 'blinding' and it is very important

as it prevents anybody mistakenly imagining that there are difference in your health or the health of your baby just because they know you had a particular vaccine.

Remember, the group you and your baby are in is picked by chance. You cannot decide and we cannot decide either.

Delivery and newborn vaccines

It is very important that you intend to deliver at Sukuta or Faji Kunda health centres. We will keep in close contact with you once you are in the study and the study team will see you alongside the staff in the antenatal clinic when you come for visits. We may also telephone you to see how you are doing and can visit you too if you like.

It is very important that you let us know if you are coming to the health centre for delivery. We will also make sure study staff are at or near the delivery room at the health centre all the time. Once your baby has delivered we will collect a sample of blood from the umbilical cord (after it has been separated from you and your baby). Rarely less than a teaspoon (3mL) sample might need to be taken from your baby with a needle if the sample cannot be obtained from the cord. We will collect a 5mL (1 teaspoon) blood sample from you.

Your newborn baby will be examined by a study doctor after birth to check that they are healthy and to identify any problems. Following this they will be given the vaccines that all newborns in The Gambia should receive after birth (BCG, hepatitis B vaccine, oral poliovirus vaccine drops). On the day of your randomisation, your baby will be already allocated (by chance also) to receive the acellular or the whole cell type of the pertussis vaccine at the normal time for EPI vaccines, which is at 2, 3 and 4 months.

Home and clinic visits after vaccination

After the vaccines given to you during pregnancy, you will be observed for about half an hour. If there are any concerns you might be seen by a study doctor in clinic. You will then be visited daily at your home for three days by a member of the field team to check that you remain well. The field worker will ask you some questions, look at the site the vaccines were given and check your temperature. A week after these vaccines you will be seen at the study clinic in all cases.

Clinic visits

Your baby will next be seen at 2, 3, 4 and 5 months to receive the recommended vaccines according to their study group and to have some extra blood tests done which will allow us to study how the baby's immune system responds to the 2 different types of whooping cough vaccines.

The baby will have a 1 teaspoon (5mL) blood sample taken at 2 and 4 and 5 months, and then another sample at one other day of the week following the vaccination at 2 and 4 months, determined by a lottery envelope. The study team will also give all the routine EPI vaccines during these visits. We will record these on your baby's Infant Welfare Card. It is very important that you do not also have these vaccines at the EPI clinic and we will remind you of this when we see you.

Some groups of babies will also have nasal secretions collected at the same scheduled visits as the blood sample collection. We don't yet know if your baby will fall into these groups, as it depends on the original group you are assigned to while you are still pregnant, and they were determined by the lottery envelope. Nevertheless, we would already like to tell you about it now. If your baby is allocated to the nasal secretion group, 2 types of samples may be taken from inside your babies nose, around 1-hour after last breastfeeding:

1. Nasal "paper" absorption (nasosorption): A small strip of absorbent material that looks and feels like soft blotting paper will be used to absorb moisture from the inside surface of the nostril. This special sterile "paper" will be placed inside your baby's nostril and left for 60 seconds before being removed. In a very small number of cases, two of these samples may need to be taken.

2. Nasopharyngeal swab: A thin swab (like a cotton-bud) will be inserted briefly to collect secretions at the back of your baby's nose and test for viruses or bacteria that may already live on the inside surface (but do not cause illness). This is a routine method used in hospitals and previous Gambian infant studies. If possible, we will try to take it from the opposite nostril to the nasal 'paper' absorption.

There is a final clinic visit at 9 months of age. At this visit a final 1 teaspoon (5ml) blood sample will be taken from your baby. Samples from your baby's nose may also be taken, as described above, depending on the group you have been assigned to. At that stage we will also take another sample from you to see if the immunity against whooping cough from the vaccine you had in pregnancy is still measurable. This will help us decide if women will need a whooping cough vaccine with each pregnancy.

If the research study needs to be stopped or we feel that your inclusion in the research may not be best for you or your baby we will discuss this with you and you will have your normal medical care in The Gambia

What should I do if I am unwell or my baby is unwell?

If you or baby is unwell during the study it is very important that you contact the study team. This can be done by telephone and we will give you telephone numbers to contact us at any time (day or night and at the weekend). During the normal working week you can also visit the clinical trial site. If your baby is unwell with a high fever (38.5°C or more) he/she will have a blood sample (less than 1 teaspoon - 3mL) taken to look for infection and also a test for malaria. You or your baby might also need other tests, including blood tests or an x-ray picture of the chest looking for infection. These will be explained to you at the time and we will check whether or not you agree. Treatment you or your baby need according to standard good medical practice in The Gambia will be provided by the study team. If you think you are in labour you should go straight to the delivery suite at the health centre while also contacting the study team.

What will happen to the samples taken in this study?

Some of the samples collected during the study will be processed at the MRC laboratories in Fajara. Certain tests cannot be undertaken in The Gambia and will be sent to laboratories outside The Gambia for processing. If you agree, any samples remaining at the end of the study may be stored by the MRC in The Gambia or our collaborators in Europe and could be used for other research in the future which aims to benefit the people of The Gambia. No information which could identify you or your baby (e.g. your name or address) would be given to anybody using any samples. If you do not want the samples to be stored, you can tell us on the form and can still take part in the main study. Genetic tests such as tests looking at conditions which can be passed from mother or father to a baby (like sickle cell disease) and if the genes also influence immunity to vaccines could be undertaken on samples in the future, but you can tell us on the form if you don't want this to happen.

What harm or discomfort can you expect in the study?

The whooping cough vaccine has already been given to many thousands of infants and adults across the world, including in The Gambia, and is considered to be very safe, also in pregnancy. Nonetheless, when you or your baby receive any vaccine, including the routine EPI vaccines, you could have a reaction to it. Such reactions might include local pain or swelling at the injection site. You might also feel tired or unwell in other ways. Infants may feed less well, may vomit or have diarrhoea and may also be unwell in other ways. Both you and your baby could also have a raised temperature. Severe allergic reactions can also occur and can be life-threatening although reactions like this are extremely rare. We are doing the study to see how safe and effective the whooping cough vaccine is in pregnancy and compare the responses to the whole cell and acellular vaccine given to the babies to understand how best to predict the vaccine efficacy long term. While the information which already exists makes significant harm very unlikely, we will be monitoring the safety on mothers and babies as an important part of the trial including looking at the effects of the vaccine in pregnancy on the newborn baby. If any problems do occur with your pregnancy we will do our best to find out the reasons for this. This might include taking additional laboratory tests or photographs although we would discuss this with you at the time. Taking a blood sample causes mild discomfort at the time and can result in a small bruise. Taking the nasal samples may cause your baby to sneeze, wriggle or start to cry. However, the methods we are using are very safe and not painful, having been studied in many babies previously and also in The Gambia. The tools are also adapted to the small size of infants and will be used in a gentle way by trained field workers.

What benefits can you expect in the study?

We know the whooping cough vaccines being used are safe and effective at preventing the disease in babies, but we do not yet know whether giving the vaccine during pregnancy will influence with the way babies respond to their own whooping cough vaccines in the first few months of life. This question has already been studied with one type of the whooping cough vaccine (acellular) but not with the other, and we would like to find out the answer to this question. So far it appears that giving the vaccine to women in pregnancy does not change the immunity babies get from their own whooping cough vaccines. The results of the study could have a major impact on the way these vaccines are used in the future and by taking part you will have played an important part in this.

We will not contact you with any results specific to your baby. However, our team plans to organise special community open days for all participants, to discuss the overall findings from the GaPs trial. Our results will also be published in scientific journals and presented at scientific conferences, but you and your baby's privacy will be completely protected, and will not be identified in any reports.

Whichever arm you are allocated to in pregnancy, you will receive a tetanus vaccination with the aim of making sure you are both well protected against this infections and the study team will ensure that all other recommended vaccines are given to your baby in a timely fashion.

Will you be compensated for participating in the study?

You will not get paid for participation. Your transport costs to the clinic will be reimbursed and you will be provided with a mobile phone and/or credit so that you are able to contact the study team at any time if you have concerns. Any treatment that you or your newborn baby need during the study, according to standard good clinical practice in The Gambia, will be provide by the study team. You will not need to pay for this.

Are there other products or treatment?

If you do not wish to take part in the study, you and your newborn baby should receive the recommended routine EPI vaccines provided by the government clinic.

What happens if you refuse to participate in the study or change your mind later?

You are free to participate or not in the study and you have the right to stop participating at anytime without giving a reason. This will not affect the normal medical care that you receive from the government clinic. If you decide to withdraw, any information and samples collected prior to withdrawal will continue to be used and the data generated will be included in the final analysis. Your safety and the safety of your baby are our primary concern and we will encourage you to allow us to complete the planned safety follow-up even if you withdraw from other aspects of the study. If any new information becomes available during the study that may affect your participation, you will be informed as soon as possible.

If you are injured in the study what compensation will be available?

We will be responsible for providing treatment caused by procedures undertaken as part of the research study and you will not need to pay for this. This cover is provided through clinical trial insurance. If you have an unwanted reaction or other problem, we will treat you or refer you as needed. If medical treatment is required as an emergency, please refer to your health centre or clinic and contact the member of the field team who gave his/her telephone number to you or contact: (TBC)

How will personal records remain confidential and who will have access to it?

All information that is collected about you will be kept strictly confidential. Your personal information will only be available to the study team members and might be seen by some rightful persons from the Ethics Committee, Government authorities and sponsor. This could include organisations outside The Gambia. Anybody outside the study team who might see such information would only do so to ensure the study was being conducted properly.

Who should you contact if you have questions?

If you have any queries regarding the study you can contact Dr Ebrima Kanteh on 7714481, and you can always call the personal numbers of the study staff given to you. If you have any concerns you can also contact staff at your health centre or clinic. Please feel free to ask any question you might have about the research study.

Who has reviewed this study?

This study has been reviewed and approved by a panel of scientists at the MRC and by the Gambia Government/MRC Joint Ethics Committee, which consists of scientists and lay persons to protect your rights and wellbeing and The Medicines Boards of The Gambia Government.

CONSENT FORM

Screening Number: |_|_|_|_|_|_|_|_|_|_|

[Printed name of participant - expectant mother]☐ I have read the written information **OR**☐ I have had the information explained to me by study personnel in a language that I understand*
and I:-

- confirm that my choice to participate is entirely voluntarily,
- confirm that I have had the opportunity to ask questions about this study and I am satisfied with the answers and explanations that have been provided,
- understand that I grant access to data about me to authorised persons described in the information sheet,
- have received sufficient time to consider whether to take part in this study,
- agree to take part in this study.

Cross (X) as appropriate

I agree to further research on my samples/my baby's samples as described in the information sheet

Yes ☐ No ☐

I agree to genetic tests being conducted on my samples/my baby's samples as described in the information sheet

Yes ☐ No ☐

Signature/thumbprint of participant

Date_____
Time

Printed name of impartial witness*:

Signature of impartial witness*_____
Date*_____
Time*

I attest that I have explained the study information accurately in _____ and that the information was understood to the best of my knowledge by the subject's parent and that he/she has freely given consent to participate [*in the presence of the above named impartial witness]

Printed name of person taking
consent:_____
Signature of person obtaining
consent_____
Date (dd/mmm/yyyy)_____
Time (24 hour clock)

* Only required if the participant is unable to read or write.

A copy of this informed consent document must be provided to the participant.