Guy's and St Thomas' NHS Foundation Trust

Bile acid Effects on fetal Arrhythmia Study

You are being invited to take part in a medical research study. Before you decide whether or not to take part it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully. You may find it helpful to discuss it with someone else, for example a family member or friend. If there is anything that is not clear or if you would like more information, please contact us – our details are given at the end of the 'Quick Summary'.

Quick Summary

- **We are studying a condition of pregnancy called intrahepatic cholestasis of pregnancy (ICP) that is not only sometimes unbearable for women because of the itching that accompanies it but in severe cases is associated with premature labour, fetal distress and stillbirth.**

- **We want to understand more about why some babies are at risk. To do this we will use a portable device, called a Monica AN24, which can be used to record the baby's heartbeat. The monitor also records from the mother's heart. At the same time as using the Monica AN 24 we also use another very small device called a Zephyr which will tell us the positions you have been sleeping in. The Zephyr will help us to correctly analyse the mother and baby's heartbeat.**

- **You are being asked to consider taking part either because you have ICP or because you are having an uncomplicated pregnancy, and you are expecting only one baby.**

- **The study will include: having your baby's heartbeat recorded, having your own heartbeat recorded, having your sleeping position recorded, donating some blood samples to us and, if possible, letting us have some blood from you at the time of birth and some cord blood samples after your baby is born.**

Study Team contact details

If you require any further information about this study or have any questions you can contact:

Principle Investigator (insert name): XXXXX (insert email address) XXXXX
Jenny Chambers, Clinical Trial Coordinator: jenny.chambers@imperial.ac.uk – 07843 660349

The purpose of the study

For some years we have been studying ICP, also known as obstetric cholestasis (OC), a liver disorder of pregnancy that causes the woman to itch. This itching can sometimes be so bad that the mother-to-be cannot sleep at night. ICP can also lead to fetal distress, premature labour and, in very severe cases, stillbirth.

In ICP the liver is unable to work as effectively as it normally does and this leads to a build up of bile acids in the blood. It is thought that bile acids may have a detrimental effect on the baby's heart and cause it to beat with an abnormal rhythm or rate (called an arrhythmia), and also on the womb. This may explain why there is a risk of stillbirth or premature labour in some ICP pregnancies.

These changes in the heart rhythm are so subtle that they are not likely to be detected by CTG monitoring, which is the conventional method to check a baby's heart beat during pregnancy. However, they might be detected by performing an ECG (electrocardiograph) of the baby's heart using a device called the Monica AN24. This involves placing sticky tabs (electrodes) that contain harmless electrodes on your abdomen. These tabs are about the size of a small plaster, and are similar to those used on a CTG. They won't harm you or your baby but they are sensitive enough to pick up the different rhythms of your baby's heart. To help us correctly analyse the results of the ECG, we will also need to detect the positions you are sleeping in whilst wearing the Monica AN24. To do this we will also use a device called a Zephyr which is a very small device and is placed on the bottom of your breastbone using similar sticky tabs.

In order to be certain that any findings are due to ICP rather than other causes, it is important that we also study uncomplicated pregnancies to establish the normal rhythm of baby's heart at different times during pregnancy.

Why have I been chosen?

If you have ICP

We would like to invite you to join our study as a woman who has a pregnancy complicated by ICP. We plan to recruit at least 200 women with the condition.

If you don't have ICP

We would like to invite you to take part as someone who does not have ICP. We need to make sure that any results we find in the women with ICP aren't also found in women with uncomplicated pregnancies. In research terms this is referred to as being a 'control'. We plan to recruit a minimum of 200 women without any complications of pregnancy such as ICP.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do you will be given this information sheet to keep and will be asked to sign a consent form. You will be free to withdraw from the study at any time, without giving a reason, and it will not affect your care.

What will happen to me if I take part?

If decide to take part in the study, we would like to perform the following procedures.

Once you have consented to take part:

- You will have blood tests to check your liver function and to measure your bile acid levels. We will also take an extra sample of blood for research purposes – this will be used to study substances, such as hormones, in the blood that are of specific interest in ICP. In total we will take two tubes of blood (approximately 10-20 ml or three tea spoonfuls).

- Following the blood tests, the Monica AN24 ECG device and Zephyr position monitoring device will be fitted to your abdomen and the bottom of your breastbone. You will be asked to wear the Monica AN24 and Zephyr at the same time for up to 24 hours. You will be able to shower/bath as normal and we are advised that it is comfortable to wear in bed when you sleep.

- You will receive clear instructions on how to remove both monitors and will be able to remove them at home the following day. We will discuss with you how and when to return both devices to us.

- **If you have ICP**, we would like to repeat the blood tests and ECG every week from the time you are diagnosed with ICP until the time that your baby is born. However, we know that this may not always be

easy for you to do so if you can't manage more than once or prefer to only have this procedure performed just once that will still be valuable to our study.

- **If you don't have ICP,** we will give you the option of how many ECG's you would like to have performed. Even if you prefer to only have one ECG, it will still be valuable to our study.

- After your baby is born we would like to be able to collect a cord blood sample to measure bile acids and other metabolites, such as hormones. This will be collected after the placenta has been delivered so there is no risk of any harm to your baby.

All data and samples that are collected as part of this study will be stored in the research team's laboratory at King's College London. Original copies of questionnaires and consent forms are stored in a locked filing cabinet in a locked room, and electronic data are stored on a study specific, password protected database (www.medscinet.net). Data will be stored for a maximum of 10 years.

We would like to ask your permission to use your data and any remaining samples in future ethically approved studies into ICP performed either by our research group, or other groups that we work closely with, both in the UK and abroad.

What are the possible disadvantages and risks of taking part?

Apart from giving a blood sample, which may cause some mild initial discomfort, there should be no disadvantages to you in taking part in the study. The Monica AN24 device and Zephyr device should not be uncomfortable to wear and should not stop you doing anything you normally do. We will not be able to give you any results of your baby's ECG during until after your baby is born as we will not analyse the data immediately.

If when the data is analysed we detect anything in the ECG that means further action is necessary (such as scanning your baby's heart because we think we may have picked up a problem) we will talk to you about this and take appropriate action to ensure you and your baby have whatever treatment is needed.

There is **no** risk to your baby from any part of the study.

What are the benefits of taking part?

There is no intended direct clinical benefit to you and your baby from taking part in the study although we may be able to detect whether you or your baby had any ECG abnormalities whilst you were taking part in the study. Because we do not immediately analyse the readings from the machines we will only be able to disclose these results after your baby is born. In these circumstances, we will talk to you about what we have found and take whatever action is needed to ensure you or your baby receive the appropriate treatment.

Information from the study may ultimately help doctors better understand how to manage ICP and, if the device is shown to be useful, may mean that all women with severe ICP will be able to have fetal ECGs in the future.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Please contact: Principle Investigator (insert email): XXXXX (insert telephone no) XXXXX.

If you have a complaint, you should talk to your research doctor who will do their best to answer your questions. If you remain unhappy, you may be able to make a formal complaint through the NHS complaints procedure. Details can be obtained through the Guy's and St Thomas' Patient Advisory Liaison Service (PALS) on 0207 1887188, address: PALS, KIC, Ground floor, North Wing, St Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH.

This trial is co-sponsored by King's College London and Guy's and St Thomas' NHS Foundation Trust. The sponsors will at all times maintain adequate insurance in relation to the study independently. Kings College London, through its own professional indemnity (Clinical Trials) and no-fault compensation and the Trust having a duty of care to patients via NHS indemnity cover, in respect of any claims arising as a result of clinical negligence by its employees, brought by or on behalf of a study patient but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. This information will be stored on a King's College London computer that complies with the Data Protection Act 1988. All samples will be coded for the laboratory work and, therefore, your name will not be linked to the sample. The only people who will be able to identify you are members of the research team. If information about your medical history is used in medical or scientific publications we will ensure that your name is not linked to the information. We sometimes send our samples to other research groups who may be outside the EU and with whom we are collaborating. Most of these studies will be related to ICP but there may be other groups investigating other conditions of pregnancy. We will discuss this with you and you will have the option not to send your samples to these research groups. Any of your samples that we send will not have any identifiable information about you on them; they will simply have a number.

What will happen to the results of the research study?

We plan to publish the findings of the research in a medical/scientific journal.

Who is organising the research?

This research study is being organised by Professor Catherine Williamson

I'd like to take part - what do I have to do now?

We will ask you to sign a consent form to say that you understand what the study involves and that you agree to participate. There are no restrictions on behaviour or lifestyle specific to any of the tests.

You will be given a copy of the information sheet and a signed consent form to keep.

We would like to thank ICP Support for their help in the design of this information sheet

www.icpsupport.org