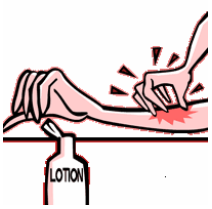
Imperial College London

OBSTETRIC CHOLESTASIS RESEARCH STUDY
PATIENT INFORMATION SHEET



You are being invited to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. The study team contact details are at the end of this information sheet.

Quick Summary of the Research

- **Around 5,500 women in the UK develop obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy (ICP)every year**
- **It's not life threatening to the woman (although the itching can sometimes be extremely distressing) but there can be problems for the baby such as fetal distress, spontaneous premature labour and, in severe cases, stillbirth**
- **Researchers are investigating several factors of OC/ICP:**
    1. **Genetics – to understand why it is seen in families**
    2. **Hormones – OC/ICP only occurs in pregnancy and usually (but not always) when the pregnancy hormones are at their highest**
    3. **Metabolites – are substances that can generally be measured in the blood and which are the end result of all the chemical changes that take place in the body on a day to day basis. Metabolites such as bile acids are thought to be the cause of problems for the baby in OC but it is possible that the condition causes high levels of other metabolites, e.g. glucose and cholesterol that may also be important**
    4. **Environment – the severity of OC/ICP can be affected by diet, taking antibiotics or viral infections**
- **Women are being asked to donate samples such as blood and urine at various points during and after their pregnancy to help scientists better understand the condition**
- **Some women who have to have surgical procedures such as CVS (chorionic villus sampling) may be asked to donate any spare tissue left over from the procedure**
- **This in turn may help doctors to manage OC/ICP pregnancies more effectively which could ultimately**

If you are currently pregnant, we realise that we are asking you to consider taking part in research at a very special time of your life and we do not wish to intrude. However, we need to recruit enough women to the study in order to make progress in our understanding of OC/ICP so we hope that you don't mind that you have been approached in this way. If you think you may wish to be involved please read on (this still doesn't commit you to anything) otherwise we thank you for agreeing to read this far and wish you all the best in your pregnancy.

If you are not currently pregnant but are interested in taking part please read on otherwise we thank you for taking the time to read this far.

The purpose of the study

We are interested in studying diseases of pregnancy (OC/ICP in particular) that can affect the health of the mother and baby. In particular we are trying to understand what genetic and metabolic factors (the chemical changes that take place in the body) can make the mother unwell during pregnancy, and which of these can also make the baby unwell when in the womb. We have been taking samples from women that include blood, urine, faeces and placenta to study these different factors.

We hope that by learning more doctors will eventually be able to offer women better treatment that helps to improve their symptoms (such as reducing the itching) and ultimately protect their unborn babies.

Why have I been chosen?

We would like to invite you to join our study as a pregnant or non-pregnant woman who has not had (or who is not expected to have) a pregnancy complicated by conditions such as OC/ICP. Women who have uncomplicated pregnancies are often referred to as 'control' groups in research. We need to include them in the study to be able to compare any significant results we may find and ensure that they apply to the disease group women only. We are aiming to recruit around 5,000 control participants.

Do I have to take part?

It is completely up to you whether or not to take part. If you choose not to it will not affect your medical care either during or after pregnancy. If you do decide to participate you will be given this information sheet to keep and be asked to sign a consent form (and one on behalf of your baby if you're pregnant). **On these forms you can indicate which samples and how many of each you are willing to let us have.**

There are generally no restrictions on behaviour, eating, or lifestyle specific to any of the tests.

What do I have to do? – During Pregnancy

There are several ways in which you can take part in the research which may include all or some of the following:

- Completing questionnaires regarding your medical and family history
- Completing a questionnaire about sleep and eating patterns as this will provide information that could help scientists discover if the times women eat and sleep make them more susceptible to developing OC/ICP
- Donating a sample of blood so that we can look at your DNA (genetic information)
- Donating some blood samples that will allow us to compare your hormones and metabolites (such as progesterone and bile acids) with women who have OC/ICP
- Donating some urine to allow us to look at hormones and metabolites
- Donating stool samples for us to look at metabolites
- Donating some tissue if you are having a procedure called CVS (chorionic villus sampling)
- Letting us have a sample of the fluid that surrounds your baby (called amniotic fluid) if you are having a procedure called amniocentesis. This procedure involves drawing some of the fluid off through a needle inserted into the womb and is generally only done if your doctors thinks it is important for the safety of your baby. This rarely happens in women who are having uncomplicated pregnancies.

The DNA sample is generally a 'one off' blood sample and may help us to understand how disorders such as OC/ICP are passed down through families. We need your DNA to make sure that any genetic variants we find in OC/ICP that we think are important cannot be found in women who don't have the condition. If you are needle phobic we can take a saliva or buccal sample. Both are very easy to provide, one involves you spitting into a pot and the other involves using a soft brush to scrape some cells from your cheek.

The other samples can also be donated just once or, if you are willing, can be given to us several times during your pregnancy to form what we call 'serial samples'. Collecting serial samples will help to give us a 'picture' of an OC/ICP pregnancy and we hope that by obtaining a record of the pregnancy in this way we may be able to pinpoint where in pregnancies disorders such as OC/ICP cause problems. We need comparison serial samples from women without OC/ICP. We will ask you to consider allowing us to have at least three serial samples but just one sample will be very valuable to us. The amount of blood we will take is small – approximately 10 ml of blood which is less than two teaspoons.

At the same time we take blood from you we will ask you to provide a urine sample in the standard urine containers that you are given by the midwives. We would also appreciate at least one stool sample from you (three samples in total during the pregnancy if possible). We will discuss how to collect this when we recruit you to the study.

Occasionally we may ask you to fast for these comparison samples as they can give a different result compared to non-fasting samples.

Some women (with or without a history of OC/ICP) may have procedures such as CVS (chorionic villus sampling) in their pregnancy and we may ask them if we are able to have any spare tissue that is left. This is because research as shown that bile acids may affect the placenta and scientists want to have a better understanding of the placenta in early pregnancy.

You can tell us at any stage in your pregnancy that you wish to stop donating samples and it will not affect your medical care.

When you have your baby we would also like you to consider donating the following comparison samples for after he or she has been born when the cord has been cut and the placenta delivered. Taking these samples cannot harm you or your baby

- Cord blood samples for DNA and metabolites
- A small piece of umbilical cord if required (for example if we are unable to obtain cord blood)
- Placenta to look at how your placenta compares to one from someone who has had OC/ICP
- The very thin membrane that surrounds the placenta called the amnion
- Urine for metabolites (we can spin the nappy to obtain some urine)
- Stools samples (also taken from the nappy)

You can donate all or some of these samples and it may be that we will only need some samples such as cord blood or placenta. We will discuss this with you when you are due to have your baby. You can either consent to this in advance or wait until nearer the time of delivery if you are happy for us to have some or all of these samples – it is up to you.

What do I have to do? – After Pregnancy

We may ask women who have had OC/ICP to let us have some samples when they are not pregnant. Samples such as blood, urine or stools taken at this stage may help scientists to learn more about what happens to the metabolites and hormones after pregnancy or before the woman develops OC/ICP in a subsequent pregnancy and may help researchers better understand how the condition develops. This could mean that new ways of diagnosing the condition early might be identified and treatments developed to prevent OC/ICP occurring. We will also need comparison samples from women who have not had OC/ICP but you are not under any obligation to have to do this.

What are the possible disadvantages and risks of taking part?

Apart from giving the blood samples, there are no disadvantages of taking part in the study. Having the blood sample taken may involve some discomfort to you, but this will be minimal. There is no risk to your baby from any part of the study.

We will not be able to give you personally any specific results from this study. However, you should be aware that there is a possibility that your results may produce an unexpected result that may need further investigation or monitoring (for example we may check your lipids (fats) which may be high and require further investigation from your GP). If this happens we will discuss this with you and, if necessary, provide any support that you may require, such as advising you to contact your GP, if appropriate, or arranging follow-up tests and/or treatment.

What are the benefits of taking part?

There is no intended direct clinical benefit from taking part in the study. However information from the study may give knowledge in the future about OC/ICP that could help doctors treat the condition more effectively and perhaps even prevent the risk of stillbirth from the condition.

What if something goes wrong?

Imperial College London is sponsor for this study and holds insurance policies which apply to it. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Chief Investigator, Professor Catherine Williamson 0207 594 2176. The normal National Health Service complaint complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Office.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. This information will be stored on an Imperial College 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. This means that your samples are what are called 'linked-anonymised' and the codes to link the sample to you are kept in a log book that is retained in a locked cabinet. 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. With your permission, we will let your GP know that you are taking part in the study but no information you provide us with will be passed on to him/her. We sometimes send our samples and data to other research groups we are working with but who may be outside the European Union (EU). Their data protection laws are not always as stringent as those within the EU but any samples sent to them are linked-anonymised (they simply have a number on them) and any data given to them will not contain any information that could possibly identify you.

What will happen to the results of the research study

We plan to publish the findings of the research in a medical/scientific journal. It is possible that we may identify something that has implications for you, for example, a genetic change that may cause you to be at risk of another liver disease, such as gallstones or which means there are certain drugs you should avoid because they may harm your liver. In this instance we will be able to contact you to let you know about this. If you do not wish us to be in contact you will be able to mark this on the consent form.

Who is organising and funding the research?

This research study is being organised by Professor Catherine Williamson who is currently funded by The Wellcome Trust but who has been funded in the past by several organisations, including Action Medical Research, Wellbeing for Women, Genesis Research Trust and The Medical Research Council.

Study team members - If you require any further information about this study, or you have any questions you can contact the following research team members: *Insert details of contacts here:*

Thank you for taking the time to read this information sheet and, if you choose to, taking part in this study