Austin Health

MERCY
HEALTH & AGED CARE

Version: 4
Date: 20/11/07

Participant Information and Consent Form

Project Title:
Comparison of (pathological) hyperfiltration of diabetes and (physiological) hyperfiltration of pregnancy.

Principal Researcher: Prof George Jerums, Head of Endocrinology, Austin Health

Associate Researcher(s): Dr Jenny Huynh

Prof Michael Permezel

Dr Sianna Panagiotopoulos

Dr Christine Houlihan

Dr Richard MacIsaac

Dr Kathy Paizis

Dr Peter Eizenberg

This Participant Information and Consent Form is 7 pages long. Please make sure you have all the pages.

1. Your Consent

If you have diabetes and an Austin Health patient and are planning a pregnancy, we invite you to take part in the clinical study looking at kidney function in pregnancy.

This Participant Information document contains detailed information about the research project. Its purpose is to explain to you as openly and clearly as possible all the procedures involved in this project before you decide whether or not to take part in it. Please read this Participant Information carefully. Feel free to ask questions about any information in the document. You may also wish to discuss the project with a relative or friend or local health worker.

Once you understand what the project is about and if you agree to take part in it, you will be asked to sign the Consent Form. By signing the Consent Form, you indicate that you understand the information and that you give your consent to participate in the research project. You will be given a copy of the Participant Information and Consent Form to keep as a record. If this information sheet contains words or information that you do not

understand, please ask the study staff for an explanation. Do not sign the consent form unless you have received satisfactory answers to all your questions.

2. Purpose and Background

The purpose of this project is to examine the kidney function of diabetic patients during pregnancy. It will involve both the Austin Hospital and the Mercy Hospital for Women.

In early diabetes, the kidneys undergo a change whereby they filter more substances (ie. hyperfiltrate) than normal healthy kidneys. This hyperfiltration is harmful to the kidneys and is thought to be a predictor of future permanent kidney damage related to diabetes. In pregnancy, the kidneys undergo a similar change of hyperfiltration, but in contrast to diabetes, this has not shown to be harmful to the kidneys of healthy, non-diabetic, pregnant women.

In addition to hyperfiltration, the kidneys also enlarge in diabetes and in normal pregnancy. Whereas the kidneys return to normal size after pregnancy, the kidneys remain enlarged in diabetes for a much longer period of time.

The filtering state of the kidneys will be measured by inulin clearance, which involves injecting inulin (a sugar substance) into the bloodstream, and then taking 2 blood samples at various times after the injection. Inulin has been widely used overseas for measurement of kidney function, and is often referred to as the gold standard of measuring kidney filtration. However, due to drug shortages, it is not readily available and is currently not licensed for routine use in Australia. To that extent, the use of inulin in this study is considered experimental.

There are currently no easy blood tests to measure kidney filtration in pregnancy. A newer blood test, cystatin C, has recently been proposed as being accurate enough to use in pregnancy to measure kidney filtration. However, this approach has not been validated for use in pregnancy.

The main purpose of this study is to determine if:

1. hyperfiltration of diabetes is additive with hyperfiltration of pregnancy
2. cystatin C can accurately measure kidney filtration in pregnancy
3. kidneys enlarge to the same extent in diabetic pregnancies compared with healthy pregnancies.

The results of this research may be used to help researcher ***Dr Jenny Huynh*** to obtain a postgraduate degree in Doctor of Medicine.

3. Study population

This study will be performed in 3 groups of pregnant women:

Group 1: Non-diabetic controls (15 participants in total)

Group 2: Women with type 1 diabetes (30 in total)

Group 3: Women with type 2 diabetes (15 in total)

These women will be those who have chosen to have their antenatal care performed at the Mercy Hospital for Women.

4. What will I have to do to take part?

All participants will attend a total of 4 or 5 test visits and have the same investigations performed.

The test visits are as follows:

Test Visit 1 – Prior to becoming pregnant (if applicable)

Test Visit 2 – During 1st trimester (i.e. between 6-12 weeks pregnant)

Test Visit 3 – During 2nd trimester (i.e. between 18-20 weeks pregnant)

Test Visit 4 – During 3rd trimester (i.e. between 32-34 weeks pregnant)

Test Visit 5 – 3 months after delivery

During all visits, you will have your blood pressure, height, weight measured, as well as your insulin regimen & duration of diabetes (if applicable) and age documented. You will also have blood (15mL) collected at each visit as well as a 24hour urine collection. The collected urine samples will be destroyed by routine practices of DLM after testing. The blood tests will be used to measure kidney function. We will check your blood sugar level to confirm whether or not you have diabetes. If the result is high and you are not known to have diabetes, it does not necessarily mean that you have diabetes, and further investigations may be required. We will discuss this with you and arrange further follow up if you wish.

Routine test samples will be handled by the Department of Laboratory Medicine (DLM) at Austin health, and will be destroyed after testing. HbA1c will be measured by DLM as part of routine diabetes care during pregnancy. Trial test samples (blood samples) will be used for testing inulin and cystatin-C. Part of the blood samples will be stored at -80°C for up to 3 years in the Endocrine laboratory, Austin Health, for measurement of hormones that may cause hyperfiltration. Samples will be coded and archived samples will be destroyed by incineration after the completion of the study.

In visit 1, 3 and 5 only, you will have your kidney size and filtering state measured. These will be performed on the same day, and you will be able to go home once the procedure is completed.

The filtering state of the kidneys will be measured by inulin clearance, which involves injecting inulin into the bloodstream, and then taking 2 blood samples at various times after the injection. The rate at which the inulin is cleared from the blood will determine the filtering state of the kidneys. The results from the non-diabetic women will be compared with those from the diabetic pregnant women. This will allow us to determine whether pregnancy has a further hyperfiltering effect on the kidneys of diabetic patients who become pregnant.

Kidney size will be measured by an ultrasound machine, which is the same machine used for routine antenatal care. This will help us see whether the kidney size in patients with

diabetes is greater than normal, healthy pregnant patients.

If you decide to take part in the study, you will be asked to come to the clinic for an initial screening visit to see if the study is suitable for you.

At the screening visit you will:

- Sign a consent form to participate in the study
- Be asked questions about your health and your usual medications
- Undergo a physical examination

After the screening visit, if you are eligible to participate in the study, you will be asked to return to the clinic within 4 weeks for Test Visit 1.

5. What are the possible risks of taking part in this study?

The study may involve unknown or unforeseen side effects.

Drug side effects
Inulin is very well tolerated. It is a sugar substance found in nature and has been used to measure kidney filtration for over 70 years. In its 70 years of use, there has only been one case of a serious allergic reaction. It has also been used before in pregnancy with no reported side effects to mother or baby.

Risks of study procedures
Venous blood samples will be taken regularly through the study. The risks associated with drawing of blood include some pain/bruising at the site of needle puncture, and on rare occasions fainting, light-headedness and infection. Your body will quickly make up for this small blood loss.

6. Are there any possible Benefits

It is not known whether there will be a benefit to you as a participant in this study. However, the study will benefit the scientific community by adding to our understanding of the changes that pregnancy has on diabetic patients and may in the future help to better counsel diabetic patients who are keen to become pregnant. In addition, if we are able to show that cystatin C can predict the filtering state of the kidneys, this simple blood test can in the future replace more cumbersome tests for measuring the filtering state of the kidneys during pregnancy, and help to diagnose kidney diseases more rapidly and easily.

7. Privacy, Confidentiality and Disclosure of Information

Any information obtained in connection with this project and that can identify you will remain confidential. It will only be disclosed with your permission, except as required by law. All the data that are collected will be stored in a file. All subjects taking part in the study will be given a coded number to ensure that confidentiality is maintained. Numbered files will be stored in a locked filing cabinet in a secure location and will be accessible only to members of the research team.

All participants have a right to request correction of information held about them by Austin Health. You will also be welcome to access any of the information collected about you if you wish to do so. Data will be kept for 15 years after which time they will be put through a

paper shredder. You will not be identified in any material that is published in journals or presented at scientific meetings, only group data will be presented.

It is possible that the results of the study will be published in the scientific literature. In any publication, information will be provided in such a way that you cannot be identified.

Your blood tests will be archived in a freezer at -20°C. These will also be de-identified, to ensure confidentiality is maintained.

8. New Information Arising During the Project

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information. This new information may mean that you can no longer participate in this research. If this occurs, the person(s) supervising the research will stop your participation. In all cases, you will be offered all available care to suit your needs and medical condition.

9. Results of Project

If you wish to know the results of the study they will be made freely available to you when you contact the Principal Investigators (see below).

10. Do I have to take part?

No, your participation in this study is entirely voluntary. You have the right to refuse participation and your routine medical care will not be affected in any way. If you agree to take part, you have the right to withdraw from the study at any time without giving a reason. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with the Austin Hospital or Mercy Hospital for Women.

The study doctor can stop your participation in the study at any time without your consent for any of the following reasons:

- If you fail to follow directions for participation in the study
- If it appears harmful to you
- If it is discovered at a later date that you do no meet the study requirements or if the study is cancelled

You will be asked questions about your experience with the study. You may also be asked to cooperate in having whatever laboratory tests and physical examinations the study doctor considers necessary for your safety.

11. Further Information or Any Problems

If you require further information or if you have any problems concerning this project (for example, any side effects), you can contact Prof George Jerums (Principal Investigator) or Dr Jenny Huynh (associate researcher) on phone 03 9496 5489 or page via Austin Hospital switch board 03 9496 5000.

13. Injury

<u>In the unlikely event that you suffer an injury as a result of participating in this research project, hospital care and treatment will be provided by the public health service at no extra cost to you.</u>

12. Other Issues

If you wish to contact someone, independent of the study, about ethical issues or your rights, you may contact Mr Andrew Crowden, Chairperson Austin Health Human Research Ethics Committee, Telephone 9496 2901

13. Ethical Guidelines

This project will be carried out according to the *National Statement on Ethical Conduct in Research Involving Humans* (March 2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interest of people who agree to participate in human research studies. The ethical aspects of this research project have been approved by the Austin Research & Ethics Committee as well as the Mercy Health and Aged Care Research Ethics Committee (MHAC-REC).

14. Reimbursement for your costs

You will reimbursed for all travel and parking expenses.

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Consent Form to Participate in Research

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I, ...…have been invited to participate in the above study which is being conducted under the direction of Professor George Jerums (Principal Investigator)**.** I understand that while the study will be under his supervision, other relevant and appropriate persons may assist or act on his behalf.

I have read and I understand the Participant Information version 4 dated 20 November 2007. I freely agree to participate in this project according to the conditions in the Participant Information.

I will be given a copy of the Participant Information and Consent Form to keep.

The researcher has agreed not to reveal my identity and personal details if information about this project if published or presented in any public form.

Participant's Name (printed) ……..

Signature Date

Name of Witness to Participant's Signature (printed) ……..

Signature Date

Researcher's Name (printed) ……..

Signature Date

Note: All parties signing the Consent Form must date their own signature.

One copy to be given to participant,
One copy filed in participant's medical record