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PARTICIPANT INFORMATION AND CONSENT FORM

Determining Dietary Phenylalanine Requirements during Different Stages of Gestation in Healthy Pregnant Women

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Sponsors: **Canadian Institutes of Health Research (CIHR)**

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available 24 hours per day and seven days per week

Site: *Oak Street Campus, UBC*
Child & Family Research Institute

1. INVITATION

You are being invited to take part in this Master's research project as there is currently little information available regarding protein nutrition during pregnancy. Pregnancy is a critical time that necessitates sufficient nutrition to ensure healthy development of both the mother and the baby. Amino acids are the building blocks of protein, which are used to build muscle and body tissue and support the immune system. Some amino acids, including phenylalanine, must be obtained in the diet, and cannot be produced in the body. It has yet to be determined the requirements for this amino acid during pregnancy. Inadequate protein intake during pregnancy has been linked to future risk of high blood pressure, heart disease and other metabolic problems in the baby. Therefore it is important to know how much phenylalanine we need to eat during pregnancy.

2. YOUR PARTICIPATION IS VOLUNTARY

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving. Before you decide, it is important for you to understand what the research involves. This consent form will tell you about the study, why the research is being done, what will happen to you during the study and the possible benefits, risks and discomforts. If you wish to participate in this study, you will be asked to sign this form.
Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide. If you decide to participate in this study, you will be asked to sign and return this form within 7 days.

3. WHO IS CONDUCTING THE STUDY?

The study is being conducted by the Child and Family Research Institute, University of British Columbia – Principal investigator Dr. Rajavel Elango. The University of British Columbia has received funding from the Canadian Institutes of Health research (CIHR) for the work required in doing this clinical research. Financial compensation to researchers for conducting the research is associated with obligations defined in a signed contractual agreement between the researchers and the sponsor. Researchers must serve the interests of the participant and also abide by their contractual obligations. For some, the payment of financial compensation to the researchers can raise the possibility of a conflict of interest. You are entitled to request any details concerning this compensation from the Principal Investigator.

4. BACKGROUND

Even though it is well known that pregnant women require more protein in their diet than non-pregnant women, it is not known exactly how much additional protein is required. Older techniques used to measure how much protein humans need required participants to eat a low protein diet for several days at a time. Because this is unethical to do in pregnant women, there is very little information available about protein (and amino acid) requirements in pregnant women. To gain a better understanding of phenylalanine requirements throughout pregnancy we plan to study pregnant women aged 20 – 40 years, in early and late pregnancy using a modern technique called the direct amino acid oxidation (DAAO) technique. This modern technique involves the consumption of protein shakes composed of specific amounts of phenylalanine mixed with a stable isotope tracer. The stable isotope tracer is a labeled amino acid, which is colorless, odorless, tasteless, and is completely safe; they are present in the air we breathe, water we drink, and food we eat. Amino acids are made of mostly ^{12}C, a kind of carbon, however the isotope tracer contains ^{13}C, a different kind of carbon. The tracer can be detected in breath and urine samples with special equipment because it looks different than the rest of the amino acids in the body. This allows us to measure if you are eating enough phenylalanine for protein synthesis to take place in your body. This technique has been used previously in healthy babies, children, and pregnant women.

5. WHAT IS THE PURPOSE OF THE STUDY?

The purpose of the study is to determine the phenylalanine needed from the diet during early (13 to 19 weeks gestation) and late (33-39 weeks gestation). Approximately 30 pregnant women will be enrolled in the study.

6. WHO CAN PARTICIPATE IN THE STUDY?

You may be able to participate in this study if:

- ☐ You are 20-40 years of age
- ☐ You are pregnant with a single child
- ☐ You are between 13-19 weeks of gestation or 33-39 weeks of gestation
- ☐ You are free of chronic diseases/acute diseases, and have a full range of physical mobility

7. WHO SHOULD NOT PARTICIPATE IN THE STUDY?

- ☐ Women who are not pregnant
- ☐ Women who are pregnant with more than one child (this changes amino acid demands)
- ☐ Women with history of spontaneous abortion or pre-term birth
- ☐ Women not in good health or have a metabolic, neurological, genetic, or immune disorder, including gestational diabetes, preeclampsia, pregnancy-related anemia or pregnancy related jaundice
- ☐ Women who are claustrophobic (we will place a clear hood, which can easily be removed, over your head for approximately 20 min to measure your energy expenditure).
- ☐ Women who are substance dependant (i.e. alcohol, cigarette, illicit drugs)
- ☐ Women who are allergic to eggs and egg protein
- ☐ Women who have severe nausea/vomiting throughout their pregnancy

8. WHAT DOES THE STUDY INVOLVE?

Overview of the Study

This study will be conducted at the Oak Street Campus of UBC at the Child and Family Research Institute (CFRI). If you agree to participate in this study, you will be asked to complete the procedures described below.

There will be one preliminary study in each gestational stage (early and late pregnancy) to ensure your eligibility to participate in the study. Each preliminary study will require approximately an hour of your time.

Following the preliminary study, you may participate in 4 separate study days, 2 in early and 2 in late pregnancy. Each of these study days will be 8 hours in length and will involve hourly meals (protein shakes and cookies) and non-invasive breath and urine sampling. A blood sample (1 tablespoon) will be collected at the Children's and Women's biochemical laboratory at the 6^{th} hour of each study day. If you choose to participate in all 4 study days, you will be asked to dedicate a total of approximately 34 hours of your time to the study.

If You Decide to Join This Study: Specific Procedures

a. **Preliminary Study Day Procedures:**

- ☐ A preliminary assessment is done to collect basic information about you, make sure you are informed about the study details, and to collect information about you to design the study diet specifically to meet your body's energy needs.

- ☐ The preliminary assessment will be conducted at the Clinical Research Evaluation Unit (CREU) at the Child and Family Research Institute located in BC Children's Hospital.

You will be asked to come at approximately 8 AM after having fasted overnight (10-12h). We will be measuring your body's energy needs (metabolic rate) during a resting state, thus eating breakfast or drinking coffee/tea would have an effect on the metabolic rate. The preliminary assessments will take approximately 1 hour to complete.

- ☐ During the preliminary assessment, a graduate student (M Ennis) will measure your weight, height, blood glucose, body fat, muscle mass, and resting metabolic rate, which tells us how much energy your body needs. Blood glucose will be measured using a glucometer that reads the amount of sugar in your blood by gently pricking the finger. Body fat will be estimated by measuring skin-fold thickness of the arm and shoulder using a caliper (a handheld instrument that gently pinches your skin between two moving arms). Body muscle will be measured using bioelectrical impedance which measures the passage of a small, safe amount of current (that cannot be felt) between four electrodes on the arms and legs while you lay still for a few minutes. The body fat and muscle measurements are completely safe and do not cause any discomfort or harm. Metabolic rate is measured using an indirect calorimetry machine, which consists of a clear hood that is placed over your head while you lay on a bed. The hood can easily be removed and you can see everything through the hood and breathe normally without any discomfort. This measurement takes about 20 minutes to complete. We will collect a urine sample to test whether any glucose, ketones, leucocytes, nitrile, protein or blood are present in your urine. This will be measured using a dipstick. The urine will be collected in a urine hat in the privacy of the washroom.

- ☐ You will also be asked health related questions to assess your medical history. If you are not taking pre-natal vitamins, we will provide you with some at this time.

- ☐ We will also collect information about your regular diet by questionnaire. Based on this information we will prescribe a standardized diet for the two days prior to each study day, which will ensure you meet your required protein intake. The foods will be chosen based on the foods you commonly eat.

b. **Study Day Procedures:**

- ☐ The study day will be conducted in the Clinical Research Evaluation Unit (CREU) at the Child & Family Research Institute (CFRI) located in BC Children's Hospital and each study day will take approximately 8 hours. You will be asked to come at approximately 8 AM after having fasted overnight (10 - 12 h).

- ☐ Only **water** may be consumed prior to and during the study day. The study day test diet will provide your daily energy and nutritional needs. At the end of the study day, you are free to resume your normal food intake.

- ☐ On the study day a graduate student (M Ennis) will measure your weight and height, resting energy expenditure by using the same indirect calorimetry machine that was used at the pre-assessment.

- ☐ You will eat a test liquid diet as eight small hourly meals on the study day. Each meal is made up of 1) a mixture of amino acids, 2) an amino acid-free flavored liquid and amino acid-free cookies that provide energy and other nutrients, and 3) the labeled amino acid is added to the last four meals. The test meals will meet all your daily energy, vitamin and mineral needs, as they were determined during the preliminary assessment.

- ☐ To measure how your body responds to the test diet we will collect 9 breath samples and 6 urine samples during each study day. To collect breath you will have to breathe into a container - just like blowing through a straw into a bag. Urine will be collected in a urine hat in the privacy of the washroom. We will test the amount of protein in the first and last urine sample collected during the study day. This will be measured using a dipstick. A single blood sample will be collected at hour 6 by the biochemical lab at BC children's hospital. If any results from the blood and urine tests are above or below normal you will be referred to your primary physician. We will provide you with a letter to be taken to your physician explaining your study results. If you prefer that we forward the letter directly, then we would need your primary care physicians contact information.
- ☐ When we are not collecting samples, you can watch television, listen to music, read, or bring computer to work on etc. We prefer that you stay in the temperature controlled unit for the duration of the study to ensure stable results from our study.

9. WHAT ARE THE POSSIBLE HARMS AND DISCOMFORTS?

There are no known risks involved with participating in this research, either to you or the fetus. Some women may find the finger prick used for blood glucose measurement uncomfortable. Some women may, during the study day, find having nothing to eat other than the prescribed drinks and protein free-cookies to be challenging. There may be a small amount of bleeding when blood is taken from the vein. The blood draw might feel uncomfortable, result in feeling faint, lightheaded or dizzy and might cause some minor bruising, or rarely an infection at the site of the blood draw. The blood samples provided by you will not be used for any purposes other than the research in this study. We recognize that the length of the study day, and travel to BC Children's Hospital might pose an inconvenience for you.

10. WHAT ARE THE POTENTIAL BENEFITS OF PARTICIPATING?

There are no direct benefits to you from taking part in this study. However, we hope that the information learned from this study can be used in the future to improve dietary phenylalanine and protein intake recommendations during pregnancy.

11. WHAT IF NEW INFORMATION BECOMES AVAILABLE THAT MAY AFFECT MY DECISION TO PARTICIPATE?

You will be advised of any new information that becomes available that may affect your willingness to remain in this study.

12. WHAT HAPPENS IF I DECIDE TO WITHDRAW MY CONSENT TO PARTICIPATE?

Your participation in this research is entirely voluntary. You may withdraw from this study at any time and without providing any reasons for your decision. If you decide to enter the study and then withdraw, there will be no penalty or loss of benefits, if any, to which you are otherwise entitled.
If you choose to enter the study and then decide to withdraw at a later time, all data collected about you during the enrolment part of the study will be retained for analysis, after which the study information may be shredded.

13. CAN I BE ASKED TO LEAVE THE STUDY?

The study investigators may decide to discontinue the study at any time, or withdraw you from the study at any time. If you are not able to follow the requirements of the study or for any other reason, the principal investigator may withdraw you from the study. If the principal investigator considers withdrawal to be in your best interest to ensure your health (e.g. in the case of an acute illness, including gestational diabetes), you will be withdrawn from the study without your consent. In the case of blood glucose values being outside the normal range (>5.3 mmol/L), you will be provided with a letter that can be given to your primary care Physician.

14. WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his or her designate by representatives of by representatives of the UBC Research Ethics Boards for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a participant in this study. Only this number will be used on any research-related information collected about you during the course of this study, so that your identity [i.e. your name or any other information that could identify you] as a participant in this study will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

15. WHAT HAPPENS IF SOMETHING GOES WRONG?

Signing this consent form in no way limits your legal rights against the sponsor, investigators, or anyone else, and you do not release the study doctors or participating institutions from their legal and professional responsibilities. In the event something does go wrong BC Women's Hospital is in close proximity to the study unit, and additional medical treatment can be made immediately accessible to you.

16. WHAT WILL THE STUDY COST ME?

Participation in the study will not cost you anything. In appreciation of the time that it takes to complete this study you will receive $100 upon each study day completion up to a maximum of $400 for 4 study days. If you were recruited during the late stage of pregnancy, you will only be able to participate in two study days, for a maximum of $200.

17. WHO DO I CONTACT IF I HAVE QUESTIONS OR CONCERNS ABOUT MY RIGHTS AS A PARTICIPANT?

This study will be fully explained to you, and you will be given the opportunity to ask questions. If you have questions or want more information about the study procedures before or during participation, you may contact Dr. Rajavel Elango at any time at 778-986-8655

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598)

18. PARTICIPANT CONSENT

My signature on this consent form means:

- ☐ I have read and understood the participant information and consent form
- ☐ I have had this study explained to me, read this form and understand the information concerning this study.
- ☐ I have had sufficient time to consider the information provided and to ask for advice if necessary.
- ☐ I have had the opportunity to ask questions and have had satisfactory responses to my questions.
- ☐ I understand that all of the information collected will be kept confidential and that the results will only be used for scientific objectives.
- ☐ I understand that my participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time without giving any reason(s) and my decision to withdraw will not change in any way the quality of care that I receive.
- ☐ I understand that signing this consent form in no way limits my legal rights against the sponsor, investigators or anyone else.
- ☐ I understand that there is no guarantee that this study will provide any benefits to myself.
- ☐ I understand that if I have any further questions or desire further information I should contact Dr. Rajavel Elango at 604 – 875 – 2000 x 4911
- ☐ I understand that if I have any concerns about my rights as a research participant or my experiences while participating in this study, I may contact the toll free Research Participant Complaint Line at any time at 1-877-822-8598 or via e-mail to RSIL@ors.ubc.ca.
- ☐ **Optional:** I agree that the study investigators may re-contact me to participate in follow up studies, which will arise from the current study results.

I will receive a signed copy of this consent form for my own records.

I, _____ voluntarily give consent for my participation in the
(Participant. Please print your name)

research study entitled:

Determining Dietary Phenylalanine Requirements during Different Stages of Gestation in Healthy Pregnant Women

_____	_____	_____
Signature of Participant	*Printed Name*	*Date*

_____	_____		
Signature of person obtaining consent	*Printed Name*	*Study Role*	*Date*