Emory University
Consent to be a Research Subject and HIPAA Authorization

Title: Educational, Social Support, and Nutritional Interventions and Their Cumulative Effect on Pregnancy Outcomes and Quality of Life in Teen and Adult Women with Inborn Errors of Metabolism.

Principal Investigator: Rani H. Singh, PhD, RD, LD; Department of Human Genetics

Study-Supporter: This varies each year and is always from multiple sources, including: grants, camp fees, donations, parent group sponsors, and fundraisers.

If you are the legal guardian of a child who is being asked to participate, the term "you" used in this consent refers to your child

Introduction
You are being asked to participate in a medical research study. This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

Study Overview
The purpose of this study is to better understand the effectiveness of the education provided through the Metabolic Camp in females with inborn errors of metabolism. You are being asked to volunteer for this study because you are a female with an inborn error of metabolism. Inborn errors of metabolism interfere with the body's ability to use certain nutrients to maintain healthy tissues and produce energy.

The purpose of the Metabolic Camp is to study the effectiveness of teaching teens and young women with inborn errors of metabolism about nutrition, their disorder, and the importance of staying on diet before and during pregnancy. In addition, the pregnancy follow-up will include case reports comparing the pregnancy outcomes in women with Phenylketonuria (PKU) who attended Metabolic Camp and women with PKU who have not attended the Metabolic Camp.

If you decide to participate in Metabolic Camp Research, we may ask you to complete the following procedures during camp:

Study Procedures
- Blood collection
- Pregnancy follow-up

- Urine collection
- Stool collection
- Genotyping
- Focus groups
- Neuropsychological testing
- Neurological testing
- Bone density test (DXA)
- Bioelectrical impedance (BIA)

Blood Collection:
Blood samples will be collected at the beginning and the end of the camp week. Blood draws will collect approximately 35 cc, or about 2 tablespoons, of fluid. You will be asked to arrive at each study visit in a fasting state starting at midnight (12 AM) that morning, if possible, or for, at least, two and a half hours.

The blood draw is a simple procedure done by tying a tourniquet around your arm to make the vein noticeable. The blood is then drawn from the vein with a needle. We may look at the levels of amino acids, levels of proteins, vitamins, minerals, fats, hormones, neurotransmitters (brain chemicals) and markers of inflammation, oxidative stress (a state when your body doesn't properly handle damaging molecules), metabolomics (thousands of small molecules, which are the end products and intermediates of metabolism; e.g., amino acids, hormones, vitamins) and bone health in your blood.

When your blood is collected, we may obtain blood for filter paper spots using the same needle. The blood for the spots will be taken from a syringe after the blood is drawn from your vein or a finger stick. The blood spots or blood may be used for future studies, for example in comparing the amino acids results (blood Phe levels) from different methods of analysis.

Pregnancy Follow Up:
If you become pregnant, we would like to ask you questions about your pregnancy. We will also ask your permission to obtain copies of some of your medical records and some of your baby's medical records. We may ask you for a picture of your baby.

Urine Collection:
We may collect a urine sample. We will instruct you on how to do this properly. In the collected sample, we may look at markers of oxidative stress (a state when your body doesn't properly handle damaging molecules), creatinine, a chemical that your body naturally produces that will let us know how hydrated you are and other substances specific to PKU or MSUD metabolism. A urine sample may also be used to test an at-home monitoring device for phenylalanine levels.

Stool Collection:
We may collect a stool sample. We will instruct you on how to do this properly. In the collected sample, we will investigate the composition (what is in there) and functional groups (what they are doing) of the bacteria of the human colon (gut microbiome) by extracting bacterial DNA from the collected stool samples, analyzing it, and matching the analyzed bacterial DNA sequences to known bacterial species.

Pregnancy Testing:
You may be asked to provide a urine or blood sample for pregnancy testing. The amount of blood estimated for the overall blood draw above will not increase (see **Blood draws** on page 2). We will use blood that has already been collected.

Genetic Testing:
In order to learn more about the different gene mutations causing PKU, Maple Syrup Urine Disease (MSUD), and other inborn errors of metabolism we may obtain one of the following samples:

1. Saliva sample: this sample is collected by spitting into a container that we provide you.
2. Cheek cell sample: this sample is collected by brushing the inside of the cheek with soft brushes for 20-30 seconds.
3. Blood sample: this sample is collected in the way the other blood samples are collected. Approximately 10-15 cc or 2-3 teaspoons will be taken by venous puncture for the purposes of genetic testing.

These samples will be used to find out the specific type of gene mutation you have related to PKU, MSUD, or other inborn error of metabolism. This test will be done only one time during the study.

Focus Groups:
We may explore the knowledge, perceptions, attitudes and challenges associated with PKU or MSUD, such as healthcare transitioning, in focus groups. Focus groups will allow you to discuss your personal experiences and ideas with a small group of 6-10 fellow camp participants and will be led by a trained facilitator. Focus group sessions will take place for approximately one hour.

Neuropsychological Testing:
An interviewer, a paper-based questionnaire, or a computer will ask you questions. You will be asked to define words, identify relationships among a series of pictures, count boxes, and other tasks. You may be asked to complete computer tasks which ask you to do things such as hit a key when you see a certain sequence of number or to sort cards of different colors and shapes. This testing will last approximately 15-45 minutes per study visit.

Bone Density Test: Dual Energy X-ray Absorptiometry (DXA):
This is a test to determine the amount of lean muscle and fat your body has. It will also tell us your bone density. For this test, you will be asked to lie still on a padded medical table while a machine scans your body from above. You may be asked to wear a hospital gown for the procedure, which we would provide to you. You may be asked to hold your breath for a few seconds during the procedure. You will be exposed to a small amount of X-ray radiation (0.01 mSv); however this is just $1/10^{th}$ of the radiation dose you would get from a standard chest X-ray. The procedure will take about 20-30 minutes and will be conducted once during the week of camp. The test can be stopped at any time if you feel uncomfortable for any reason.

Body Composition: DXA and Bioelectrical Impedance (BIA)
The DXA procedure detailed above will likewise be able to measure your body composition (percent of fat tissue and percent of lean tissue) at the time of your scan. You will not need to do anything extra for DXA body composition. Another way that we may measure your body composition is with BIA. For BIA, you would stand on a device that looks like a small weight scale. It will use a small current to measure the ratio of fat and lean tissue in your body. The entire procedure should not take more than 5 minutes. The current is too small to feel and is safe.

<u>Risks and Discomforts</u>
The risks of drawing blood are minor. The common side effects include mild discomfort, bruising, or swelling at the site of the needle entry, all of which quickly go away. The less common risks associated with a blood draw are dizziness and fainting after the blood is taken, and very rarely infection. There might be slight discomfort to the inside of the mouth from using a brush to obtain cheek cells.

When you have your bone density test (DXA Scan), you will be exposed to a small amount of X-ray radiation (0.01 mSv), however this is just $1/10^{th}$ of the radiation dose you would get from a standard chest X-ray. The DXA scan cannot be

done if you are pregnant. The principal risk associated with a radiation dose to you or the fetus is the possibility of developing a radiation-induced cancer later in life. The risk for radiation-induced cancer from this study is negligible.

There may be other long-term effects of DXA scans on your health which we do know about at this time. Scans are not necessary for your medical care and will occur because you participate in this study.
You may feel uncomfortable when the body measurements are taken. You may also feel uncomfortable answering questions about words, pictures and color tests. Some women may experience anxiety from discussing a pregnancy that may have been unintended, ended in abortion, or was a difficult experience in terms of following the prescribed medical diet.

There is always a remote risk of a loss of confidentiality. It is unknown if there are social risks such as insurability and employability due to the research for which the leftover blood samples saved for future, unknown research are used. There may be other things that can happen which we do not know at this time.

New Information

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Benefits

This study is not designed to benefit you directly. Your PKU or MSUD may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about nutrition and low Phenylalanine/Leucine diets. This research may help you to develop an extended support network. You will share experiences and make new friends with other women who have PKU or MSUD. This research may help to develop diet self-management skills through taste testing, development of new recipes, educational tools and curriculum for better compliance. This research will not only benefit you but also other children with PKU or MSUD. This camp program will enable us to develop resources for other patients with PKU or MSUD for optimum nutritional control and compliance. The study results may be used to help others in the future.

Compensation

You will not be offered payment for being in this study.

Other Treatment Outside this Study

If you decide not to enter this study, there is care available to you outside of this research. You may choose not to volunteer in the whole study or in parts of the study, and it will not affect your current or future treatment. However, all participations in the Metabolic Camp Protocol are required to complete a 3-day diet record and to have blood collected to check amino acid levels at the start and end of camp. The study doctor will discuss these options with you. You do not have to be in this study to be treated for PKU or MSUD.

Confidentiality

Emory will keep any research records that it creates private to the extent that this is required to do so by law. Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Medical Record

If you are or have been an Emory Healthcare patient, you have an Emory Healthcare medical record. If you are not and have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study. Copies of the consent form/HIPAA authorization that you sign will be put in your Emory Healthcare medical record.

Emory Healthcare may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory Healthcare medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

Emory does not control results from tests and procedures done at other places, so these results will not be placed in your Emory Healthcare medical record. They will likely not be available to Emory Healthcare to help take care of you. Emory does not have control over any other medical records that you may have with other healthcare providers. Emory will not send any test or procedure results from the study to these providers. If you decide to be in this study, it is up to you to let your health providers know.

The researchers will not be looking at the results of these tests and procedures to make decisions about your personal health or treatment. For this study, those items include: Amino Acid levels, and any other test performed by a research laboratory illness and medication logs. The study staff will send a copy of your lab results and any significant abnormal findings on the admission physical to you or your parents/guardian and subject's Primary Care Physician.

HIPAA Authorization

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

PHI that will be Used/Disclosed:

The PHI that we will use and/or disclose (share) for the research study includes

- Your entire medical records
- Your medical history
- Laboratory test results
- Information relating to plasma amino acid levels and diet

Authorization to Use PHI is Required to Participate:

By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not authorize the use and disclosure of your PHI for the study, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

Purposes for which your PHI will be Used/Disclosed:

We will use and disclose your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry

out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information that is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require use to report child abuse or abuse of elder or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

People that will Use and/or Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- Emory University Clinical Research Network Staff
- Emory University Clinical Center Staff
- Emory University Hospital Staff
- Children's Healthcare of Atlanta at Egleston Staff
- Emory University Clinical Research Network Statistician or Statistician hired by researcher
- Laboratory personnel at the Emory Genetics Laboratory; Emory University Hospital Laboratory; Children's Healthcare of Atlanta Laboratory; LabCorps, and Maine Medical Center Reach Institute
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research
    - Government agencies that regulate the research including: Office for Human Research Protections and the Food and Drug Administration
    - Public health agencies
    - Research monitors and reviewer
    - Accreditation agencies

Expiration of Your Authorization
This authorization will not expire because it is a research study.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must write to: Dr. Rani H. Singh; Emory University School of Medicine; Department of Human Genetics; 101 Woodruff Circle 7th Floor, Suite 7130 Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know

Not all people and entities are covered by the Privacy Rules. HIPAA only applies to healthcare providers, healthcare payers or healthcare clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy Rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your healthcare providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations and/or for other purposes besides this study.

In Case of Injury

If you get ill or injured from being in the study, Emory would help you to get medical treatment. Emory has not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proved that your injury or illness is directly caused by the negligence of an Emory employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this trial, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Rani Singh at telephone number 404-778-8519. You should also let any health care provider who treats you know that you are in a research study.

Costs

There will be no costs to you for participating in this study, other than basic expenses like transportation and camp registration. You will not be charged for any of the research activities.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the clinical staff or researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interest;
- You were to object to any future changes that may be made in the study plan;
- You did not follow the rules of the study;
- or for any other reason.

Contact Information

Contact Mary Lauren Salvatore, the study's Research Coordinator at Phone: (404)-778-8527
or Dr. Rani H. Singh the study's Principal Investigator at 404-778-8519:

- if you have any questions about this study or your part in it,

- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Opting-In to Participation in Blood and Urine Sample Storage:
With your permission, leftover blood and urine samples may be saved for future, unknown research. These blood samples will be labeled with participant ID number, date, and study number. The samples may be shared with other investigators. You can refuse to have your samples stored and still be able to participate in the study.

_____ (initials) I **do** agree to allow my blood and urine samples to be stored for future testing, including DNA (genetic) testing

_____ (initials) I **do not** agree to allow my blood and urine samples to be stored for future testing, including DNA (genetic) testing

Even if you **do** agree to allow your blood and urine samples to be stored for future testing, at a later date you may request that samples be destroyed. If you want to revoke this permission you must write to: Dr. Rani H. Singh; Emory University School of Medicine; Department of Human Genetics; 101 Woodruff Circle 7th Floor, Suite 7130 Atlanta, GA 30322.

Consent
Please print your name and sign below if you **agree to be in the Metabolic Camp research study.** By signing this consent form, you will not give up any of your legal rights. We will give you a copy of the signed consent to keep.

_____
Name of Subject

_____ _____
Signature of Subject (if 18 years of age or older) Date Time

_____ _____
Signature of Legally Authorized Representative Date Time
with authority for research decisions (if subject under 18 years of age)

_____
Authority of Legally Authorized Representative or Relationship to Subject

_____ _____
Received Informed Consent Form Date Time