COVER PAGE

Study Title: Enhanced Early Nutrition for Preterm Infants to Improve Neurodevelopment and Minimize Metabolic Risk

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CONSENT FORM

Enhanced Early Nutrition for Preterm Infants to Improve Neurodevelopment and Minimize Metabolic Risk Consent Form

You are invited to participate in a research study of enhanced early nutrient delivery to preterm infants. Your child was selected as a possible participant because he/she was born prematurely (<32 weeks gestation) weighing less than 1500 grams (approximately 3 pounds, 5 ounces). We ask that you read this form and ask any questions you may have before agreeing to be in the study.

This study is being conducted by Dr. Sara Ramel MD (Department of Pediatrics, Division of Neonatology) and Dr. Ellen Demerath PhD (Division of Epidemiology and Community Health); all at the University of Minnesota. It is funded by the University Of Minnesota Department Of Pediatrics.

Study Purpose

Preterm infants can experience poor growth while in the Neonatal Intensive Care Unit (NICU) that persists for years after discharge home. This poor growth can have a negative impact on long term development. In addition, rapid catch-up growth later in childhood can impact long-term health. The purpose of the study is to determine if giving increased amounts of intravenous (IV) nutrition early in life will improve growth and development for infants born prematurely.

There are two groups of patients in this study. One group will receive standard IV nutrition per NICU protocol. The second group will receive higher amounts of calories, proteins and fats during the first week of life via the Study protocol. This is how we hope to find out if enhanced nutrition can improve growth and development for babies born prematurely.

We will use a computer program to randomly place your infant into one of these two study groups. This means we will put your infant into a group by chance. It is like flipping a coin or drawing names out of a hat. Your infant will have an equal chance to be in either group. In the case of twins, both will be placed in the same group.

This study will follow both growth and developmental outcomes. Specifically, we will look at whether this nutritional intervention can increase length growth and lean mass (muscle) gains, along with weight gain. We will also specifically look in your baby's blood to see if increased early nutrition affects growth factors and if there is a relationship between this nutritional intervention, improved growth, increased growth factors and improved brain development.

Infants who are born small and undergo catch-up growth are at risk for gaining weight faster than length. This can put them at higher risk for becoming overweight and developing heart disease later in life. Early gains in length and lean mass, but not fat mass, have also been associated with improved development. This study aims to increase lean mass gains through increased nutrition and possibly improve long-term health and developmental outcomes.

Infants randomized to the study protocol will start on higher initial amounts of calories, proteins and fats. They will also undergo faster increases of these nutrients during their first week of life. Routine labs will be monitored via the NICU protocol and nutrient provision will be adjusted if intolerance is noted.

Once your infant is stable and able to be disconnected from respiratory support and IV's we will begin to measure their body composition weekly. The Pea Pod uses changes in pressure within a chamber to determine your infant's body volume. Combined with weight and length, this allows us to determine your infant's body composition (fat and lean tissue mass). The Pea Pod is non-invasive, safe and accurate.

We will also use Event Related Potentials (ERP) tests to look at early markers of your infant's ability to learn at 2 time points after hospital discharge (~40 weeks and 4 months of age corrected for prematurity). The ERP tests involve placing monitoring patches on their head to record babies' brainwaves while they experience sounds and pictures, which are familiar and new. ERP tests are safe and non-invasive and are no more bothersome than washing an infant's hair or allowing them to play with toys. These visits will be coordinated with other routine outpatient visits whenever possible or desired.

Study Procedures

If you agree to participate in this study, we would ask you to do the following:

<u>While your child is a patient in the hospital:</u>

- During the first week of life your baby will receive IV nutrition either via the standard NICU protocol or via the Study protocol; which nutrition protocol your baby is on will be randomized, as described above. Members of your baby's care team will be blinded to which group your baby is in. This means they will not know which group your baby was assigned. If the care team needs to know which group your baby is in for your baby's care, the study team can tell them Typical clinical labs will be monitored and nutritional intake will be adjusted accordingly.
- Once your baby is stable and breathing room air without assistance, he/she will undergo weekly body composition assessment using air displacement plethysmography (PeaPod). Briefly, the PeaPod measures changes in pressure within a chamber to determine your infant's body volume. Combined with weight and length, this allows us to determine your infant's body composition (fat and lean tissue mass). Therefore, during the body composition measurements, your baby's current weight and length will be entered into the Pea Pod. Your baby will then be placed in the chamber of the Pea Pod for approximately two minutes to calculate your baby's body volume. The chamber of the Pea Pod is warmed, has constant air flow and a viewing window which allows the study personnel and you to see your baby throughout the test. There is no radiation (x-ray) involved in the test. Your baby will be on a monitor (heart rate and oxygen levels) throughout the test. A nurse or physician will be with your baby throughout the measurement. The Pea Pod is located within the NICU. The test can be cancelled at any time if your baby is not tolerating the assessment.

- At one week of age and at ~35 weeks gestational age, approximately 0.8 ml of blood (about 1/6 teaspoon) will be obtained via lines your baby already has (IV) or heel stick during other routine blood work. These samples will be tested for growth hormone levels. Often there is leftover blood from routine blood work that can be used for the research samples so no additional blood is needed; however, if not, we will get the minimal amounts required to do the research testing. All in-patient blood samples will ONLY be collected if your baby is having routine blood tests done. If your baby does not have any blood tests ordered for a particular week, no blood will be drawn for this study.
- Your baby will have daily weights measured and recorded by the nurse caring for your baby. A member of the healthcare team and research coordinator (RN) will measure your baby's length and head circumference weekly while in the NICU. This information will be entered into a secure database called REDCap (Research Electronic Data Capture). REDCap is a secure web application for building and managing databases, often used for research data. It is HIPAA-compliant, password protected, and only members of the study team will have access to your baby's data.
- While your baby is hospitalized information will be gathered on nutrition, clinical course and illness. This information will be entered into the REDCap database described above.

<u>After Discharge from the hospital:</u>

- Once your baby is discharged, you will be asked to complete monthly questionnaires regarding your baby's eating and sleeping habits. These will be sent out via email or a paper copy can be mailed to you if requested.

<u>At Term Corrected Age and 4 months Corrected Age:</u>
You will be asked to bring your baby back for 2 outpatient visits at the Center for Neurobehavioral Development, University of Minnesota - East Bank. These visits will include:

- Weight, length and head circumference will be measured, along with a body composition measurement using the Pea Pod. This will be the same as the measurements done while your child was in the hospital.
- Your infant will also undergo an Event Related Potentials (ERP) and visual evoked potentials (VEP) test that examines the speed at which your baby learns new information. The method that is used to perform these tests is as follows: We will place elastic net containing 128 sponge-tipped sensors on your child's head. These sensors record the electrical activity naturally produced by the brain. The net is not painful and does not use any gels or pastes to record the activity. However, the sponges are soaked in a mild salt-water solution, so your child's head will get damp during the session. When the cap is in place, your baby will lay/sit on your lap and brain activity will be recorded while your baby listens to a variety of sounds and looks at a flashing picture on the screen. This test will take approximately 15-20 minutes, including the time to put on and remove the cap.

Risks of Study Participation

The study has the following risks:

If your baby is randomized to the Study protocol they will receive higher amounts of proteins, fats and sugars. Typical monitoring labs will be monitored per the NICU protocol. Your baby may experience intolerance of these higher amounts of nutrition, specifically with higher levels of blood sugar and/or triglycerides (cholesterol). These are common findings in any baby born early and if they occur the nutrition will be decreased accordingly.

All in-patient blood samples will ONLY be collected if your baby is having routine blood tests done. If your baby does not have any blood tests ordered for a particular week, no blood will be drawn for this study. Therefore, there will be no extra pokes associated with the study.

There are no risks involved with body measurements. The Pea Pod chamber has continuous recirculation of air and very strict temperature and carbon dioxide controls. It is equipped with a variety of sensors and alarms to alert the tester of any abnormal function. The Pea Pod also allows the testing to be stopped at any time for any reason. The Pea Pod is non-invasive, safe and accurate and no more bothersome than normal daily activities such as diaper changing or bathing.

We will also use Event Related Potentials (ERP) and Visual Evoked Potentials (VEP) at the outpatient visits to look at early markers of your infant's cognitive status. There are no risks involved with cognitive testing. These tests are safe and non-invasive. They are no more bothersome that washing your child's hair or allowing them to play with toys.

Benefits of Study Participation

If you agree to let your infant take part in this study, there may or may not be direct medical benefit to your infant. If increased nutrition in the first week of life is found to improve growth and brain development, your infant may experience these benefits. Half of the infants studied will receive nutrition via our typical NICU routine and will not benefit. We hope the information learned from this study will benefit other infants who are born early in the future.

Alternatives to Study Participation

The alternative to study participation is not to participate in the study and receive routine NICU cares.

Study Costs/Compensation

You will receive a $25.00 gift card at hospital discharge, and an additional $25.00 gift card at each of the 2 outpatient visits. You will not be charged for any of the tests.

Research Related Injury

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research related injury, let the study physicians know right away.

Confidentiality

The records of this study will be kept private. Your baby's record for the study may, however, be reviewed by federal agencies that oversee human research, the investigator and research team for this study, and by departments at the University with appropriate regulatory oversight.
We will not include any information in publications or presentations that will make it possible to identify you or your baby. A copy of this signed consent form will be placed in your baby's medical record. The study information will not be recorded in the medical record and will be kept in locked areas. To these extents, confidentiality is not absolute. Study data will be encrypted according to current University policy for protection of confidentiality.

Protected Health Information (PHI)

Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

Voluntary Nature of the Study

Participation in this study is voluntary. Your decision whether or not to participate in this study will not affect your current or future relations with the University or the University of Minnesota Masonic Children's Hospital. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

Contacts and Questions

If you have questions about research appointments, the study, research results, or other concerns contact the researchers. You may ask any questions you have now, or if you have questions later, **you are encouraged to** contact them:

Researcher Name: Sara Ramel MD
Phone Number: 612-626-0644
E-mail Address: sramel@umn.edu

Research Coordinator: Mary Pat Osborne
Phone Number: 612-624-0581
E-mail Address: marypat@umn.edu

To share feedback **privately** about your research experience, including any concerns about the study, call the Research Participants Advocate Line: 612-625-1650 or give feedback online at www.irb.umn.edu/report.html. You may also contact the Human Research Protection Program in writing at D528 Mayo, 420 Delaware St. Southeast, Minneapolis, Minnesota 55455.

You will be given a copy of this form to keep for your records and a copy will go in your baby's medical record.

Statement of Consent

I have read the above information. I have asked questions and have received answers. I consent for my child to participate in the study.

_____
Printed name of Subject

_____
Signature of guardian

_____
Printed name of guardian

Date_____

_____
Signature of Person Obtaining Consent

_____
Printed name of person obtaining consent

Date_____

Are you interested in receiving the results of this study? **Yes** **No**

Do you give permission to be contacted about participating in future studies? **Yes** **No**

**If you answered yes to either question above, please provide your contact information:

_____

Street Apt. #

_____

City, State, and Zip Code

Email: _____

Phone: (_____) _____ - _____

Do you prefer to be contacted via mail, email, or phone? _____