STUDY TITLE: ***Pathophysiology of the Aerodigestive Reflex in Infants: GERD Management Trial***

Consent form for following study:

Identifiers: NCT02486263 Unique Protocol ID: 11-00734 Secondary IDs: R01DK068158

Brief Title: Neonatal Gastro-Esophageal Reflux Disease (GERD) Management Trial (GMT)

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.℠

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CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

STUDY TITLE: ***Pathophysiology of the Aerodigestive Reflex in Infants: GERD Management Trial***

PRINCIPAL INVESTIGATOR: ***Sudarshan R. Jadcherla, MD***

CONTACT TELEPHONE NUMBER: ***614-355-6643***

SUBJECT'S NAME: _____ DATE OF BIRTH: _____

Key Information About This Study

The following is a short summary of this study to help you decide whether or not to participate. More detailed information follows later in this form.

The purpose of this study is to evaluate the causes of and treatment for feeding difficulty in infants with Gastro-esophageal Reflux Disease (GERD). You are being asked to enroll your child in this study because they had a Reflux index higher than 3 on a pH/impedance test.

Study participation:
If you decide to enroll your child in this study, they will undergo an esophageal manometry test to see how well the muscles of the throat, food pipe and stomach work together. Then your child will be randomized into one of two groups. The difference between the two groups will be in feeding volumes and positons. Both groups will receive medication for Gastroesophageal Reflux. They will receive the medication for 4 weeks. After that we will repeat the manometry study and your child will have another pH/impedance test.

Study visits:
The first pH/impedance testing and manometry will take place while your child is in the NICU.
The second pH/impedance study will take place 5 weeks later. If your child has been discharged, you will be asked to bring them back to the hospital for an overnight stay.
If your child has been discharged, you may be asked to keep a diary for us until the 2nd study is scheduled
See a more detailed discussion later in this form.

The main risk(s) of the study comes from having the manometry catheter and pH/impedance catheters. These are same as when any tube is placed through the nose and can include redness, irritation and minor bleeding. There are no known risks of using the medication for GERD.

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The benefit(s) of the study are your child will receive evaluation and close observation related to GERD, feeding and breathing problems. Information known from other studies may be of benefit to your child. Your participation may add to medical knowledge about infants who are at risk of feeding difficulty due to GERD and airway disease.

If you are interested in learning more about this study, please continue reading below.

1) INTRODUCTION

We invite you to be in this research study. Using this form as a guide, we will explain the study to you. If you have any questions about the study, please ask. By signing this form, you agree to be in this study. If you do not want to be in this study, all regular and standard medical care will still be available to you here at Nationwide Children's Hospital. Participation is voluntary. You can leave this study at any time.

You will be given a signed and dated copy of the consent and the assent forms.

2) WHERE WILL THE STUDY BE DONE AND HOW MANY SUBJECTS WILL TAKE PART?

This study will be done at Nationwide Children's Hospital and we hope to enroll *120* participants.

3) WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

If you decide to enroll your child in this study, we will start by doing a manometry study. A manometry study is test to see how well the muscles of the food pipe (esophagus) work together. A special feeding tube called a manometry tube is passed through your child's nose into the food pipe. This tube is similar to the tube used for feeding babies in the NICU. This tube is then connected to a machine that measures the movement of the muscles of the food pipe.

Once the manometry tube is placed, we will test how well your baby swallows. To do this we, will put 6-8 teaspoons of room air and 3-4 teaspoons of sterile water through the manometry tube and into the middle of your baby's food pipe. We will start with small amount so of each of those things and work our way up to larger amounts. Then, we will put 3-4 teaspoons of Gerber Apple Juice into the middle of the food pipe to test how your baby handles acid reflux. Apple juice contains sugar, fiber, vitamins and is slightly acidic, but is gentler than stomach acid. To test your baby's suck-swallow coordination, we will be using a device called an N-trainer. The N-trainer uses a pacifier on a receiver to create waveforms visible on a screen that can be used to evaluate a baby's suck-swallow pattern. Another way we will evaluate your baby's suck-swallow pattern is by using small pressure sensors that are threaded into a pacifier and a nipple. These sensors are small and your baby will not be able to feel them. Finally, we will feed your baby to test how well they can eat from a bottle.
To tell when a swallow begins, the activity of the muscles of the neck will be recorded with the help of sticky leads (like chest leads) placed on the chin. To watch facial movements and behaviors during

the study and match them to what is going on in the food pipe, we will record video using a video camera.

Because GERD can affect the vocal cords, we will also take an ultrasound of the vocal cords during the manometry study. An ultrasound probe will be placed over the surface of neck. This is not an invasive procedure, and there are no risks associated with this procedure. The ultrasound gel will be wiped off at the completion of the procedure. The manometry study is recorded for approximately 3 hours.

This study is randomized. Randomized means that each subject will be picked by chance, like tossing a coin or drawing straws, to receive either the regular treatment for GERD or the new treatment.

Following the manometry study, your child will be placed into one of two groups of patients. One group will receive the current, standard treatment for GERD, which includes feeding regular volumes of formula, no restriction on how long the feed lasts, what position the baby is in during the feeding, or what position the baby is placed in when returned to his/her crib, and treatment with medication.

If your baby is placed in the second group of patients he or she will receive the following treatment: Restricted feeding volumes with increased calories, taking at least 30 minutes to finish a feed, placing the baby on his/her right side during feeds and placing them on their back once they are returned to the crib following a feed. This group will be treated with medication, too.

After four weeks of treatment, the medications will be stopped and one week later your baby will be restudied using both the pH/impedance study and manometry study. Your baby's progress will be monitored between studies by using feeding diaries and by looking at the chart in EPIC.

We will also be following your baby throughout the first year by monitoring clinic visits and phone calls to you.

Conventional Arm	Study Arm
pH\impedance study with a reflux index 3 or more	pH\impedance study with a reflux index 3 or more
Manometry testing	Manometry testing
Prilosec for 4 weeks	Prilosec for 4 weeks
No changes in how much formula your baby gets	Decrease how much formula your baby is getting, but will increase calories to make sure he\she grows
No change in how you hold your baby when you feed him\her	Feed your baby in a side lying position with their right side down
Your baby will be on Prilosec for four weeks, then the medication will be stopped	Your baby will be on Prilosec for four weeks, then the medication will be stopped.
We will repeat pH\impedance and manometry tests after 1 week off Prilosec	We will repeat pH\impedance and manometry tests after 1 week off Prilosec

4) WHAT ARE THE RISKS OF BEING IN THIS STUDY?

Babies who are in the NICU often have tubes placed through the nose for feeding. Feeding tubes are generally very safe and effective. However, even if it is placed gently, a feeding tube can irritate the nose, mouth, or stomach and cause some minor bleeding. The special tube used in our study is placed under close monitoring, and is thought to be safer and thinner than regular feeding tubes. To minimize the risk of discomfort during tube placement, we coat the tube with a water- based gel. We also use sucrose on a pacifier for calming the baby down. These are standard practices in the nursery to comfort babies. If there are symptoms during the procedure, your baby will receive medical help right away. We have done over 500 studies from different centers using this method and we have not witnessed any complications.

If you are worried about anything while in this study, please call the study doctor (Sudarshan R. Jadcherla, MD) or study coordinator (Rebecca Moore, RN, BSN) at the telephone number at 614-355-6635. There may be other risks of being in this research study which are not known at this time

5) WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?

Your child's participation is this study is voluntary. It is not necessary to participate in this study in order for you to get care for your condition.

6) WHAT ARE THE COSTS AND REIMBURSEMENTS?

It will not cost you anything to be in this study. If you decide to enroll your child in this study, you will receive a total of $50.00 to help you with any expenses that might come up as a result. The payments are in the form of a debit card with $20.00 loaded onto the card when you enroll your child and another $30.00 when your child has the second study.

All costs related to the research parts of this study will be covered by the research team. However, the parts of the study that would be done for routine clinical care will be billed to you and to your insurance company or third party payer. You may have to pay any costs that the insurance company or third party payer does not pay. The study team will discuss these costs with you.

A parking voucher will be provided to you come if it is necessary for you to bring your child back to the hospital for the second study procedure.

7) WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the procedures that are part of the Study, you should seek medical treatment for the injuries and tell the Study Doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

In most cases, this care will be billed to your health insurance company or whoever usually pays for your health care at the usual charges, but some insurance companies will not pay for care related to a study. If the care is provided at Nationwide Children's Hospital, we make no commitment to pay for the medical care provided to you. No funds have been set aside to compensate you in the event of injury. If no one else pays for your care, you may have to pay for the cost of this care. This does not mean that you give up any of your legal rights to seek compensation for your injuries.

8) WHAT HAPPENS IF I DO NOT FINISH THIS STUDY?

It is your choice to allow your child be in this study or to stop at any time. If you decide to stop being in this study, it is OK, but you must call the Principal Investigator or the study coordinator. If you stop being in the study, there will not be a penalty or loss of benefits to which you are otherwise entitled.

If at any time the Principal Investigator believes participating in this study is not the best choice of care, the study may be stopped and other care prescribed. If the study instructions are not followed, participation in the study may also be stopped. If unexpected medical problems come up, the Principal Investigator may decide to stop your participation in the study.

9) OTHER IMPORTANT INFORMATION

Nationwide Children's Hospital is a teaching hospital and we are committed to doing research. Doing research will enable us to learn and provide the best care for our patients and families. You may be asked to participate in other research studies in the future. You have the right to decide to participate or decline to participate in any future studies. We will not share your contact information with researchers outside Nationwide Children's Hospital.

10) HOW WILL MY STUDY INFORMATION BE KEPT PRIVATE?

Efforts will be made to keep your child's study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law. Your records may be reviewed by the following groups (as applicable to the research):

- Primary Investigator (Dr. Jadcherla) and study staff
- The Nationwide Children's Hospital Institutional Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human subject researc*h*
- The Food and Drug Administration (FDA)
- OSU Department of Biostatistics

If you have a bad outcome or adverse event from being in this study, the Principal Investigator and staff or other health care providers may need to look at your entire medical records.

The Protected Health Information (PHI) collected or created under this research study will be used/disclosed as needed until the end of the study. The records of this study will be kept for at least 10 years.

PHI will only be shared with the groups listed above, but if you have a bad outcome or adverse event from being in this study, the study team or other health care providers may need to look at your entire medical records.

The results from this study may be published but your identity will not be revealed.

Certificate of Confidentiality

To help us protect your privacy, the National Institutes of Health has issued a Certificate of Confidentiality for this study. This Certificate will be used to resist attempts to force us to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

The Certificate cannot be used to resist a demand for information that is used for auditing or evaluation of federally funded projects or for information that must be disclosed to meet the requirements of the Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your participation in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then we will release the information even though we have the Certificate of Confidentiality.

The Certificate of Confidentiality also does not prevent us from disclosing voluntarily, without your consent, information that would identify you as a participant in the research if required by state and/or federal law. In Ohio, if we have reasonable knowledge that a felony has been or is being committed we are required to notify state officials.

The Certificate does not protect study information that is placed into your medical records.

Future Research Use:

With your permission, we would like to store your PHI for future research purposes, and as part of such future research purposes, your PHI may be disclosed to people or entities not listed above, such as researchers not involved with this study, government agencies, research foundations, or pharmaceutical or device companies sponsoring future research. This future research may or may not be related to your medical problem. This future research may include sensitive information. Any future research projects will be reviewed and approved by an Institutional Review Board which protects the rights, welfare, and safety of human research subjects. If your PHI is used or disclosed in future research studies, absolute

confidentiality cannot be guaranteed. Information shared for future research may be shared further with others and no longer be protected by federal privacy rules.

If you decide at any time that you do not want your PHI stored for future research, you must make this request in writing to the Principal Investigator at *700 Children's Drive, Columbus, Ohio 43205*. Once we receive your written request, we will destroy your child's PHI. However, if we have already shared your PHI with another individual or entity, we will not be able to destroy any of the PHI that are no longer in our possession.

Nationwide Children's Hospital retains the right to cease storage and destroy the PHI at any time without sending notice to you or obtaining your consent.

You do not have to agree to use of your PHI for future research in order to be in this study, and your decision will not affect the care you receive from the study doctors or Nationwide Children's Hospital.

I agree to allow my child's PHI to be stored and used for future research as described above: (initial)

____ YES ____ NO

11) <u>WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?</u>

If you have questions about anything while in this study or you have been injured by the research, you may contact the Principal Investigator at _614-355-6643, Monday – Friday, between ___8:00am and 4:30 pm_.

If you have questions, concerns, or complaints about the research, questions about your rights as a research volunteer, cannot reach the Principal Investigator, or want to call someone else, please call (614) 722-2708, Nationwide Children's Hospital Institutional Review Board, (IRB, the committee that reviews all research in humans at Nationwide Children's Hospital).

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Signature Block for Children

Your signature documents your permission for the named child to take part in this research.

_____
Printed name of child

_____ _____
Signature of parent or individual legally authorized to consent to the child's general medical care — Date & Time AM/PM

_____
Printed name of parent or individual legally authorized to consent to the child's general medical care

Note: Investigators are to ensure that individuals who are not parents can demonstrate their legal authority to consent to the child's general medical care. Contact Legal Services if any questions arise.

_____ _____
Signature of second parent or individual legally authorized to consent to the child's general medical care — Date & Time AM/PM

_____
Printed name of second parent or individual legally authorized to consent to the child's general medical care

If signature of second parent not obtained, indicate why: (select one)

- ❑ Not required by IRB
- ❑ Second parent is deceased
- ❑ Second parent is unknown
- ❑ Second parent is incompetent
- ❑ Second parent is not reasonably available
- ❑ Only one parent has legal responsibility for the care and custody of the child

_____ _____
Signature of person obtaining consent — Date & Time AM/PM

_____
Printed name of person obtaining consent