NYU Langone Health

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Research Subject Informed Consent Form

Title of Study:	Cold milk as a novel therapy for dysphagia in preterm infants
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1. About volunteering for this research study

As a parent, your preterm child is invited to take part in a research study. Your child's participation is voluntary, which means you can choose whether or not you want to take part in this study. People who agree to take part in research studies are called "subjects" or "research subjects". These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what your child will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide that your child can take part in this study, you have to sign this form. We will give you a copy of this form signed by you for you to keep.

2. What is the purpose of this study?

You are being asked to allow your child to participate in a research study to evaluate if drinking cold milk (breast milk or formula at 4-9°C Temp) improves swallowing in premature babies who have swallowing dysfunction (also called dysphagia). We also want to see if feeding cold milk to babies is safe. Currently, feeding infants cold milk is not a standard practice at NYU- Langone Long Island Hospital NICU. The most prominent characteristic of dysphagia is inadequate airway protection, which can cause the milk to enter the breathing tube instead of the feeding tube to the stomach (aspiration and penetration). Aspiration is when food or liquid passes below the vocal folds, and penetration is when food or liquid enters the airway but not below the vocal folds.

This can cause significant problems in the lungs. In this study, we will evaluate if feeding cold milk for the entire feeding (up to 15 minutes) will decrease the incidence of aspiration and penetration as defined above in preterm infants

3. How long will I be in the study? How many other people will be in the study?

Your child's participation in this study may last up to 48 hours. There will be a total of 42 children enrolled in this study over a period of 2 years.

4. What will I be asked to do in the study?

You are being asked for your child to be a possible participant in this study because your child is a premature baby and is suspected of having dysphagia. Your medical team has told you that your child

requires a diagnostic test called a Video Fluoroscopic Swallow Study (VFSS), or Fiberoptic Endoscopic Evaluation of Swallowing [FEES) or both. Your medical team will explain the details of these tests. The VFSS uses X-ray to follow the pass of the milk during swallowing to see if it goes from the throat to the feeding tube (that will be normal) or if it passes to the breathing tube (that will indicate dysphagia). The FEES is a tiny scope that is passed through the child's nose and will provide a direct but limited view of swallowing function without exposure to X-ray. Performing these two procedures together will give the medical team the most complete and beneficial view of the swallowing movements. These tests (VFSS and FEES) are standard of care and are ordered by the child's medical team to help treat dysphagia. Once your medical team inform you that they are planning these tests, the research team will approach you to discuss this research.

The following study procedures will be done before the VFSS/FEES testing:

Step 1 :

- Your child will be transported to the radiology suite and undergo VFSS and or FEES, as ordered by the treating medical team. This step is considered standard of care and is ordered by your child's medical team.
- If no swallowing dysfunction is noted, the procedure will end, and your child will no longer be eligible for further participation in this research study. If dysfunction is observed, your child will be eligible to participate in the next phase of the study.
- The VFSS and or FEES will be repeated while feeding cold milk as done previously for 5 swallows. These 5 swallows assessment are done for the research purpose only. If the dysphagia didn't improve, the study would end, and your child will no longer be eligible for participation further in this research study.
- If the dysphagia improves with the cold milk, the infant will then be fed cold milk for up to 15 minutes by mouth (as much as the baby tolerates). Following the cold milk feeding, the infant will be re-assessed again by VFSS/FEES for an additional 10 swallows (These 10 swallows assessment are done for the research purpose only).
- The baby will return to the NICU accompanied by the NICU team, including the neonatologist.
- The infant's temperature and vital signs will be monitored every 10 minutes during the whole procedure. A neonatologist will be next to the baby at all times.

Step 2 (bedside procedures, done next day):

We will evaluate the infant's sucking, swallowing, and breathing patterns using a non-invasive FDA approved machine (called nfant machine). This device is in clinical use for several years and routinely used in several NICUs around the USA. It looks just like a bottle that your child will feed from, but attached to the nipple is a wireless sensor that will assess sucking and swallowing coordination during feeding. This machine is not routinely used at NYU- Langone Long Island Hospital NICU but will be available only for infants enrolled in this research study.

- The nfant tests will be completed under two feeding conditions. The first condition will be feeding the standard room temperature milk and second condition will be feeding the cold temperature milk/formula for an entire feeding (15-20 minutes or as tolerated by the baby).
- The axillary temperature (underarm) will be measured immediately prior to and after each feeding condition.
- Several non-invasive abdominal ultrasounds will be done at the bedside to assess the blood supply to the digestive system one hour before and at 30 and 60 minutes after both types of feedings (standard temperature and cold milk).

The results of the testing with cold milk will be disclosed to the medical team.

Any identifiable private information collected and/or used for the purposes of this research will not be used or distributed for future research studies.

Depending on the scheduling of the VFSS/FEES testing by the infant's medical team, the research team might need to do Step 2 before Step 1, as described above. There will be at least 24 hours period between the two steps.

5. What are the possible risks or discomforts?

Risks associated with FEES- FEES is a routine procedure done in the NICU and is ordered by the medical team. It is possible that your child may experience a little nose bleed during this procedure or breathing issues, however this risk is very low. Introduction of the scope can cause changes in vital signs including increase or decrease in respiratory rate and heart rate or decrease in oxygen blood level requiring removal of the scope. Although not reported previously, there is a chance that the introduction of the scope can cause injury to the nasal cartilage. The diameter of the FEES scope is similar in size to the nasal gastric tube that your child likely has already, which is commonly well tolerated in preterm infants, even during oral feedings. Several studies demonstrated its safety in children. The procedures is routinely done in the presence of an attending Neonatologist to ensure safety.

Cold Stress: A concern associated with feeding cold milk is the development of hypothermia (the baby getting cold). Cold stress can cause changes in vital signs including increase or decrease in respiratory rate, heart rate or decrease in oxygen blood level. Cold stress can also lead to decrease blood supply to the gut and decrease feeding tolerance. Several studies have assessed the effects of cold feeds in healthy term and healthy pre term infants, which revealed no difference in feeding tolerance or body temperature. In a small study done at NYU- Langone Long Island Hospital NICU, 12 preterm infants were fed cold milk. Infants feeding cold milk showed improved feeding coordination and all infants tolerated the feeding well with no incidence of cold stress or feeding issues. During our study we will frequently measure your child's temperature, vital signs as well as check gut blood supply using ultrasound to ensure that your child tolerates the cold feeding well.

Radiation Exposure: Your child's participation in this study will involve exposure to radiation from the VFSS. The study VFSS protocol requires only 15 additional swallows of cold milk for the research purpose. This would add an extra 18 seconds of exposure time of additional radiation exposure. This exposure is not necessary for your child's medical care, is for research purposes only and is necessary to obtain the desired medical information.

The effective radiation dose you will receive from these research scans is approximately [0.1] mSv which is less than your yearly dose from natural environmental radiation in the US (3.1 mSv) and the limits set by the FDA for individuals participating in basic research studies, which is 5mSV. According to the International Commission on Radiological Protection (ICRP), the increased risk of health effects, such as cancer, from radiation doses of this amount is either too small to be observed or nonexistent.

6. What are the possible benefits of the study?

Your child may or may not personally benefit from being in this study. The potential for scientific discovery into the swallowing mechanisms of prematurely born infants hold tremendous potential to benefit this at-

risk population. In a previous study done at NYU- Langone Long Island Hospital NICU, 12 preterm infants with dysphagia were given cold liquid for 5 swallows and assessed by VFSS. There was a significant improvement in dysphagia during cold liquid swallows. The results of this research will be disclosed to your child's medical team. If the results confirm the cold milk's benefit and safety for your child, the medical team can consider using cold milk to treat your child's dysphagia which can be of a significant benefit.

7. What other choices do I have if I do not participate?

Your child's participation in this study is voluntary. You may refuse to participate without penalty or loss of any care to your child and without affecting your child's current or future medical care at NYU- Langone Long Island Hospital Hospital. There are no alternatives to participation in this study, except that you may choose not to take part in this study.

8. Will I be paid for being in this study?

There will be no financial compensation for participation in this study.

9. Will I have to pay for anything?

There is no cost to you or your child's insurance for taking part in this study.

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay. If you have health insurance, the cost of these services will be billed to your insurance company. If your insurance does not cover these costs or you do not have insurance, these costs will be your responsibility.

10. What happens if my child is injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator's name and phone number are listed at the top of page 1 of this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

11. When is the study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped or your participation ended at any time without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The principal investigator, NIH, or other body responsible for monitoring the safety of the study has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

12. How will you protect my child's confidentiality?

Your child's medical information is protected health information, or "PHI", and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your child's research record as well as information in your child's medical record at NYU Langone Health. In compliance with NYU Langone Health policies and procedures and with HIPAA, only those individuals with a job purpose can access this information.

Medical information created by this research study may become part of your child's medical record. We may include your child's research information in your child's medical record so that other members of the NYU Langone Health community who may treat your child have access to important information about your child's health.

You have a right to access information in your child's medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to view and copy the information once the study is over in accordance with NYU Langone Health policies and applicable law.

To help us further protect your confidentiality, this research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). The NIH has issued a Certificate of Confidentiality for this research. This adds special protection for the research information (data, documents, or biospecimens) that may identify you.

Research information protected by this Certificate of Confidentiality cannot be disclosed to anyone else who is not connected with the research, without your consent. With this Certificate of Confidentiality, the researchers may not disclose or use research information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, without your consent. However, disclosure, without your consent, is still necessary if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases).

The Certificate of Confidentiality cannot be used to refuse a request for information from appropriate government agencies responsible for project oversight.

The Certificate of Confidentiality does not prevent you from releasing information about yourself and your involvement in this research, including for your medical treatment. Federal regulations may also allow for the use or sharing of information for other scientific research.

By agreeing to be in this research and signing below, you are giving your consent to share research information with others at NYU Langone Health. This means that your research information, including lab results, x-rays, MRIs, information about the investigational drug used in this study, may be included in your NYU Langone Health electronic medical record.

The clinical trial information of this study will be published at Clinical Trials.gov. ClinicalTrials.gov is a Web-based resource that provides patients, their family members, health care professionals, researchers, and the public with easy access to information on publicly and privately supported clinical studies on a wide range of diseases and conditions. The Web site is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH). Information on ClinicalTrials.gov is provided and updated by the principal investigator of the clinical study. Studies are generally submitted to the Web site (that is, registered) when they begin, and the information on the site is updated throughout the study. In some cases, results of the study are submitted after the study ends. This Web site and database of clinical studies is commonly referred to as a "registry and results database."

13. HIPAA Authorization

As noted in the Confidentiality section above, federal law requires us and our affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies your child's and relates to your child's past, present, and future physical and mental health conditions. We are asking for your permission (authorization) to use and share your child's health information with others in connection with this study- in other words, for purposes of this research, including conducting and overseeing the study.

Your child's treatment outside of this study, payment for your child's health care, and your child's health care benefits will not be affected even if you do not authorize the use and disclosure of your child's information for this study.

What information may be used or shared with others in connection with this study?
All information in your child's research record for this study may be used and shared with those individuals listed in this section. Additionally, the information in your child's medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your child's physical examinations, laboratory tests, and procedures.

Who may use and share information in connection with this study?
The following individuals may use, share, or receive your child's information for this research study:

- The research team, including the Principal Investigator, study coordinators, and personnel responsible for the support or oversight of the study
- National Institute on Deafness and Other Communication Disorders (NIDCD)
- Governmental agencies responsible for research oversight (e.g., The National Institute of Health).
- Health care providers, including your child's doctors and others who provide services to you in connection with this study, and laboratories or other individuals who analyze your child's health information in connection with this study.

What if I do not want to give permission to use and share my child's information for this study?
Signing this form is voluntary. You do not have to give us permission to use and share your child's information, but if you do not, you will not be able to participate in this study.

Can I change my mind and withdraw permission to use or share my child's information?
Yes, you may withdraw or take back your permission to use and share your child's health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, your child will not be able to stay in this study.

How long may my child's information be used or shared?
Your permission to use or share your child's personal health information for this study will never expire unless you withdraw it.

14. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. The NYU IRB Office number is (212) 263-4110. The NYU School of Medicine's IRB is made up of: doctors, nurses, non-scientists, and people from the community.

15. Who can I call with questions, or if I'm concerned about my child's rights as a research subject?

If you have questions, concerns or complaints regarding your child's participation in this research study or if you have any questions about your child's rights as a research subject, you should speak with the Principal Investigator listed on top of page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Institutional Review Board (IRB) at (212) 263-4110.

Signature of Parent(s)/Guardian for Child

I give my consent for my child to take part in this research study and agree to allow his/her health information to be used and shared as described above.

When you sign this form, you agree to take part in this research study, as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Subject's Mother or Father (Print)	Signature of Parent	Date

Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

Witness to Consent Process for Non-English Speaking Subjects (using a translated consent form OR "Short Form" in Subject's Spoken Language)

Statement of Witness

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language and that the subject was given the opportunity to ask questions.

Name of Witness (Print)	Signature of Witness	Date