Why is this research being done?

The purpose of this study is to learn more about how menstrual pain affects pain sensitivity development including at bladder and muscle sites. For more information, please see the Why is this study being done? section below.

How long will my child and I participate?

You and your child will be asked to participate in the study for two to four years which includes a Pre-Period Baseline Visit, a Period Visit 1 (approximately 3-9 months after the onset of your child's first menses) and a Period Visit 2 (approximately one year after the Period Visit 1).

What will happen to my child and me during the study?

You and your child will be asked to complete three visits to Evanston Hospital. During the visit(s), you and your child will be asked to complete questionnaires. Your child will be asked to have their bladder capacity tested, undergo a pressure pain threshold test, a cold water test, and be asked to watch videos and sounds while researchers measure their brain's activity. Your child will be asked to collect a saliva sample for analysis. Throughout the visit(s), we will record your child's breathing (using a respiratory belt), heart rhythm, and abdominal muscle activity. For more information, please see the What will happen during the study? section below.

Will my child and I benefit from the study?

We don't expect you and your child to receive any benefit from taking part in this study, but we hope to discover information that will help scientists understand why some adult women develop pelvic pain issues.

Will taking part expose my child or me to risks?

This research is considered no more than minimal risk, which means that there is no more expected risk to you and your child than what you and your child might experience during a typical day or during a routine physical exam. For details and a list of risks you and your child should know about, please see the What side effects or risks can my child and I expect? section below.

Will my child and I be paid to participate?

Payment for your child's time and parking validation are available if you and your child decide to take part in this study. For more information, please see the Will I and my child be paid for participating? section below.

Will it cost my child or me anything to participate?

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

You will not be responsible for any costs related to the research; however, you or your insurance company will still be responsible for the cost of your normal medical care. For more information, please see the Will there be additional costs? section below.

Taking part in this study may lead to unforeseen additional costs to you or your insurance company. For more information, please see the Will there be additional costs? section below.

Please review the rest of this document for details about these topics and additional things you and your child should know before making a decision about whether to participate in this research.

EXPLANATION OF STUDY:

Introduction: You and your child are being asked to volunteer for this clinical research study.

This Consent Form gives information about the study that you can talk about with your doctor and/or family. You are being given this information to help your decision. If you have any questions, you can ask the study doctor or staff.

Why is this Study Being Done?

We are asking you and your child to take part in a research study because we are trying to learn more about the development of period pain and to understand more about bladder and muscle pain in girls. This study does not provide any treatments. We plan to enroll approximately 375 female children and their parent(s)/guardian(s). Only one parent/guardian is required to participate in the study with their child. It can be either parent/guardian, however, please keep in mind we will discuss menstruation. All participants will be enrolled at NorthShore University HealthSystem (NorthShore).

What Will Happen During the Study?

This study involves 3 visits lasting about 3 hours each, at Evanston Hospital. The visit(s) may be completed in one visit or broken down into several visits depending on scheduling with our staff, you, and your child's schedule. You, as the parent/guardian, will be required to accompany your child at the beginning of their first visit so that we can review this consent form with you. You will be asked to complete a set of questionnaires about your child's behavior, pain level, sleep patterns, and a medical history form. You will also be asked to complete a sensory and pain history form for yourself at the beginning of each visit. The portion of the research session in which your presence is required will take approximately 30-minutes to 1 hour. If you have more than one child participating, we will be able to complete approximately 1 hour of both visits together (including the portion during which a parent/guardian is required to attend), but our team can only complete the remainder of procedures with one child at a time (sessions can potentially be scheduled back-to-back for your convenience).

The visit(s) will include a bladder test, pressure test, cold water test, and watching videos and listening to sounds while we are collecting data on how your child's body functions, specifically their heart, lungs, and brain. Brief home diaries reviewing your child's experience with menstruation will be recorded by you and your child beginning with your child's first period, and then every 4 months for 2 years. Each of the study procedures is described below.

Questionnaires: Your child will be asked to complete questionnaires about their pain, physical developmental stage (pubertal maturation), physical activity, and mood including questions about symptoms of stress, anxiety, positive feelings, and depression. The questionnaires will take approximately 30 minutes to complete. You will also be asked to complete questionnaires about your child's health.

You and your child may choose not to answer questions that make you or your child uncomfortable. Your child will be asked to complete the questionnaires independently. They will be instructed to contact the research team if they have any questions while completing the questionnaires. We will not share your child's results with you unless their depression and anxiety scores are abnormal.

In order to ensure privacy and reduce bias in your child's data, we ask that you step out of the room while they complete the testing. However, if your child requests that you stop by briefly during the session, you are allowed to do so.

Bladder Testing: We encourage your child to arrive well-hydrated (drinking a lot of water) for each visit.

At the start of the bladder test, we will ask your child to go the bathroom and urinate so their bladder is empty. After the bathroom break, your child will be asked to drink water and rate how their bladder feels every 15 minutes until they reach what we call "red zone" or maximum tolerance, which means they REALLY have to go to the bathroom, at which point your child will go to the bathroom and urinate into a disposable container. Throughout this task, we will also do ultrasounds of your child's abdomen to see how full their bladder is. This device takes a picture of the inside of your child's abdomen using a handheld device called a "transducer" similar to the picture below. Your child may be asked to drink more water (up to 10 ounces) if your child does not reach maximum tolerance after 45 and 60 minutes.

If your child does not reach maximum tolerance after 75 minutes, we will stop the task. All of your child's urine samples will be stored for analysis.

Pressure Tests: A trained staff person will perform the pressure tests. These tests use a specially designed pressure measuring device called an algometer. The algometer, although widely used in research, is considered investigational and has not been approved by the Food and Drug Administration (FDA). The tip of the handheld external algometer is made of rubber and about the same size as a pencil eraser. Your child will be asked to complete two pressure tasks using the algometer described below.

Pressure: In this task, we will apply pressure to your child's knee and then shoulder and ask your child to press a button the moment the pressure turns from pressure to pain (i.e., the point at which your child's pain reaches a "1" on a 0-10 pain scale).

Cold Water Test: In this task, a pressure pain threshold test will be performed again as described above on the knee and shoulder, but following a second stimulus, cold water hand immersion. After their hand is in the cold water for 20 seconds, they will remove their hand from the cold water and we will retest the knee and shoulder pressure tests. The water temperature will be maintained at 5-12° C (41-55° F).

Videos and Sounds (Sensory Testing): We will ask your child to watch videos of flashing lights and listen to sounds using headphones and tell us what they think of them. We may also ask your child to complete a brain teaser involving reading and identifying colors. During the tasks, we will ask your child to wear a recording cap for electroencephalography (EEG). It looks like a swim cap that has sensors on it. This lets us measure your brain electrical activity. Your child should not feel anything from wearing the cap. We can adjust the fit if it feels too tight or uncomfortable. We will also need to put clear hair gel in your child's hair to make the sensors work

Physiological Data: Throughout the visit(s), electroencephalography (EEG), electromyography (EMG), electrocardiogram (ECG), and respiratory belt devices will be used. The ECG and EMG involve putting stickers on your child's chest and stomach and attaching cords onto the stickers to measure the electrical activity of their heart and stomach muscles. The respiratory belt will go around your child's chest and will monitor their breathing. We will also ask to take your child's blood pressure.

Saliva: Up to 1 tablespoon of your child's saliva will be collected for analysis.

Menstrual Diaries: At home we will also ask your child to complete a brief menstrual health diary, including a survey of pelvic symptoms, amount of vaginal bleeding, and use of medications, every 4 months throughout the 2 years of follow up. This will be started with their first period, ideally. The diary will take approximately 5 minutes per day for 7 days to complete. We will work with you to determine the best way to collect this information (i.e. online, email, phone, regular mail).

Menstrual Effluent: Menstrual effluent refers to the blood flow released during a menstrual period. At the first visit, your child will be provided with a single standardized tampon (Tampax®, Pearl Junior) and instructions will be given regarding menstrual effluent collection. Participation in this portion of the study is completely voluntary and if your child does not want to participate, your child does not have to. Those who are comfortable and willing to complete this task will be instructed to call staff on the first day of their period to receive instructions on how to place the tampon. The tampon should remain in place for 4 hours to allow adequate collection of effluent. Afterwards, the tampon needs to be delivered to our lab at Evanston Hospital within 48 hours of collection for analysis. We will also repeat collection each

year that they're in the study for interested participants. This portion of the study will not be separately compensated.

During this study, the research team will collect information about your child for the purposes of this research. Your child's urine, saliva, and menstrual effluent will also be collected for analysis purposes.

How Long Will We Be In the Study?

You and your child will be asked to participate in the study for approximately 2-4 years which includes 3 visits:

1. Pre-period Baseline Visit,
2. Period Visit 1 approx. 3-9 months after starting their period and
3. Period Visit 2 approx. 1 year after the Period Visit 1.

What Other Choices Do We Have?

You and your child do not have to take part in this study.

Are There Benefits to My Child or Me for Taking Part in the Study?

This is not a treatment study. There is no direct benefit to participating in this study. You and your child may indirectly benefit by feeling that they are helping others with pain conditions in the future.

What Side Effects or Risks Can My Child and I Expect?

Questionnaires: We will ask personal questions related to your child's medical history, physical development, and mood. When filling out these questionnaires, you and your child will be reminded that any questions may be skipped.

Bladder Testing: Drinking the amount of water needed to complete the bladder testing may cause mild discomfort in your child's stomach, but it is not dangerous. We expect this discomfort should be fully relieved at the end of the bladder test when they go to the bathroom.

Ultrasound: Ultrasound of the abdomen is safe. In rare cases, your child may be allergic to the transmission gel and develop a mild rash of the skin. The gel will be washed off when the scan

is complete, so the degree of irritation should be limited even in that situation. However, you may need to seek additional treatment for your child for relief if a rash or a skin problem were to develop. The ultrasound wand against your child's abdomen may cause some pressure symptoms, although it should not be painful.

Pressure Tests: Pressure testing may cause temporary muscle soreness to your child. The discomfort is expected to be limited to the testing site and self-limited in time (we will stop applying pressure after your child reports the first sensation of pain). If your child experiences lingering muscle pain or soreness, we recommend doing whatever your child usually does for muscle pain or soreness after the visit. In case your child does not press the button by the time the pressure reaches a certain threshold, the pressure will be discontinued for safety reasons. If your child rates their pain at the time they pressed the button as higher than 2, the instructions that they should try to press the button the moment their pain reaches a "1" on a 0-10 pain scale will be repeated.

Sensory Testing: The videos and sounds may be irritating and could rarely cause a headache or nausea if your child is sensitive to light and sound. In children with epilepsy (known or unknown), the visual task could trigger a seizure. If your child does not have epilepsy, the task will not cause a seizure. In the unlikely event your child has undiagnosed epilepsy, the visual task could provoke abnormal brain activity, but the chance of such an event is estimated to be very low (6 in a 1,000,000 based on prior research studies). Our staff will keep an eye on your child and the EEG recordings during the visual task. As a precaution against a potential seizure, if we see anything abnormal, we will stop the task. In the case a rare seizure does occur despite these precautions, we can provide the EEG recordings to another physician for further evaluation. Our study does not pay for treatment for any newly diagnosed epilepsy.

The hair gel will mess up your child's hair for a little while, but can be washed out with shampoo.

Physiological Data: The EEG cap and/or ECG/EMG electrodes are painless. We can adjust the position of the EEG, EMG and ECG cords if they are bothersome to your child to make them more comfortable. Our equipment is certified to prevent any risk of electric shock. Removing the stickers from your skin can be mildly painful, similar to removing a band aid.

For any of the above listed study procedures, your child may ask not to complete any procedure that they do not want to do. They may quit a study procedure if they decide after starting it that they do not want to complete it.

Will My and My Child's Medical Information Be Kept Private?

Information from this study could be published in journals or presented at meetings. If either of these happens, you and your child's names and other personal information will not be used. The researchers running this study will try to keep you and your child's personal information private. Your and your child's study related information may be looked at by other doctors in

this study. Your and your child's research file can also be looked at by the NorthShore Institutional Review Board, other medical personnel at NorthShore who are involved in your care, funding agencies, or by the Food and Drug Administration (FDA).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Will my or my child's information be used for research in the future?

Information or specimens collected from you and your child for this research study may be used for future research studies or shared with other researchers for future research if you give us permission at the bottom of this consent form. If this happens, identifying information will be removed before any information or specimens are shared. Since identifying information will be removed, you and your child will not be asked for additional consent. You and your child's study-related information will be kept until the study is closed out.

Protected Health Information (PHI)

During this research, identifiable information about you and your child's health will be collected. In the rest of this section, we refer to this information simply as "protected health information (PHI)." In general, under federal law, PHI is private. However, there are exceptions to this rule, and you and your child should know who may be able to see, use and share your and your child's PHI for research and why they may need to do so.

Your and your child's PHI will only be used for the purposes described in this Consent Form. Your and your child's authorization for activities described in this section does not have an expiration date.

What protected health information (PHI) will be used?

- Past, present and future medical records, including information housed in the Electronic Medical Record called "Epic," which is maintained by NorthShore University HealthSystem
- Information about research procedures, including research office visits, medical tests, procedures, interviews and questionnaires

Who may see, use and share my child's or my PHI and why may they need to do so?

- NorthShore research staff involved in this study

- The NorthShore IRB board that oversees the research and the NorthShore research quality improvement program
- Federal and state agencies (such as the Department of Health and Human Services, the National Institutes of Health and other US government bodies that oversee or review research)
- A group that oversees the data (study information) and safety of this research

Some people or groups who get your and your child's PHI might not have to follow the same privacy rules that we follow. We share PHI only when we must, and we ask anyone who receives it from us to protect your and your child's privacy. However, if your or your child's information is shared outside NorthShore, we cannot promise that it will remain private.

Do my child and I have the right to withdraw permission for the use of PHI?

You and your child have the right to withdraw your permission for us to use or share your PHI for this research study. If you and your child want to withdraw your permission, you must notify the person in charge of this research study in writing.

If you and your child withdraw your permission, we will not be able to take back information that has already been used or shared with others.

Once permission is withdrawn, you and your child cannot continue to take part in this study. However, you and your child will not be penalized or lose any benefits to which you are entitled.

Do my child and I have access to our health information?

You and your child have the right to see and get a copy of your PHI that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. However, to protect the study, you and your child will not be able to see some of the study information until after the study is completed. The researchers are not required to release to you research information that is not part of your and your child's medical record.

You and your child have the right not to sign this form that allows us to use and share PHI for research; however, if you and your child do not sign it, you and your child cannot take part in this research study.

Will My Child and I Be Paid for Participating?

You and your child will be given gift card(s) as a thank you for your participation in the study according to the following schedule:

Pre-period Baseline Visit: $90 for child visit; $10 for parent

Period Visit 1: $90 for child visit; $10 for parent

Period Visit 2: $90 for child visit; $10 for parent

Quarterly Diaries: $10/month (max $70)

*If you and your child are able to make it to your first scheduled visit (at each point), you will receive an incentive bonus of $10 paid to the parent, to try and optimize careful selection of visit dates (max $30)

Total Compensation: $400

If your child does not complete the study for any reason, your child will be given a gift card for each study task that they do complete. Your child will be given a gift card even if they start a study task but do not complete it. Additionally, we will cover parking costs you incur throughout your and your child's participation.

If you have any questions regarding compensation for participation, you may contact the study team at (847) 570-2622.

Will There Be Additional Costs?

There is expected to be no additional cost to you and your child from being in this research study. You and your child will still be responsible for all costs that you or your child would normally incur as part of routine care.

What If My Child is Injured During the Study?

We do not expect injury during this study. If your child becomes hurt or sick because of being in this research study, they can get medical treatment at NorthShore. You or your health insurance plan will be billed. No money has been set aside to pay for the costs of this treatment. You can ask for more information from the Research Institute of NorthShore.

If your child scores greater than the threshold on the depression and/or anxiety subscales, you will be notified that your child's score was above average. If you and your child would like to seek further treatment, please note that your health insurance will be billed accordingly, as no money has been set aside to pay for the costs. However, we will provide the NorthShore Mental Health Services hotline number (847-570-1400) in case you and your child are interested in seeking counseling or psychiatric services, as well as useful websites for parents/guardians and children who struggle with coping and/or stress:

(https://middleearthnj.wordpress.com/2010/04/09/developing-coping-skills-in-teens/ and

http://www.copingskills4kids.net/).

Health insurance plans (including Medicare) may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

Can My Child or I Withdraw From the Study?

Your and your child's participation in this research study is voluntary. If you or your child decide not to be in this study, you and your child can still get medical care as usual. If you or your child decide to participate now, you both may leave the study at any time. No matter what decision you make, there will be no penalty to you and your child and you both will not lose any of your regular benefits.

What Are My Child's and My Rights as a Research Subject?

You and your child may get more information about your rights from the Chairperson of the Institutional Review Board (IRB). You can also call the IRB Coordinators at 224/364-7100. These are the people you should contact about any problems or research-related injuries that happen during the research study.

By participating in this research study you and your child do not waive any rights to which you both would normally be entitled.

You and your child are not required to complete any study procedure that you do not want to complete. You may leave the study at any time without penalty.

Will My Child and I Be Informed of New Information About the Study?

Any significant new information that may affect your and your child's participation will be given to you as soon as it becomes available.

Will My Child or I receive our results?

Testing in this study will be done for research purposes only and results will not be returned to you or your child or your doctor(s).