

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

Corticosteroids for Children with Febrile Urinary Tract Infections

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Who is being asked to take part in this research study?

We invite your child to take part in our research study because your child has a urinary tract infection (UTI). About 1 in 7 children with UTI will develop kidney damage (scarring). Scarring to the kidney can be caused by the swelling and irritation (inflammation) that comes with an infection. We are trying to find out if kidney scars can be decreased or prevented by using steroid medication (medicine that prevents inflammation). We plan to follow about 250 children in Pittsburgh who are 2 months to 6 years of age in this study. Please read this form carefully. As the study staff discusses this form with you, please ask them to explain any words or information that you may not understand.



What is the purpose of this study?

This research study will allow our medical team the chance to improve the care that they provide to children with UTI. Taking part in this research study is entirely your choice. Your child will receive medical care for his/her UTI, whether you allow your child to be in this study or not.

The purpose of this study is to learn if

- 1) steroids prevent kidney scarring
- 2) markers in the urine or blood can help to predict which children may have scarring
- 3) genetic testing can predict which children are more likely to have kidney scarring and
- 4) genetic testing can show which germs cause scarring along with the kidney infection.

In approximately 6 months, we will do a kidney scan (DMSA scan) to check if your child developed scars. This is an FDA-approved test used to check for kidney scarring after UTI. Blood and urine samples will also be collected to try and identify those children who are at most risk for developing kidney scarring.

What procedures will be performed for research purposes?

Your child's doctor will treat your child's UTI in the usual way with antibiotics. Neither you nor your child's doctor will know if your child will be given daily steroid (dexamethasone) or daily placebo (non-active medication). Randomization means that a computer will choose which study medication your child receives. There is an equal chance of your child receiving either one. Your child's doctor will be able to get the information about what your child is receiving in case of an emergency.

The study nurse will show you how to give your child the liquid study medication or placebo and will give the first dose of the study medication to your child no later than 48 hours after the first dose of antibiotic treatment for the UTI. You will also be shown how to give your child the study medication with a flavoring syrup with each separate dose. Pharmacies often offer flavorings to make medications more appealing to children. The study nurse will show you how to measure the medication/placebo with a dosing syringe and give it to your child by mouth. The dose of medicine depends on your child's weight (0.15 mg per dose for every 2.2 pounds that your child weighs). Your child will take the study medication or placebo (0.15mg/kg per dose) twice a day for 3 days. It is best to give the medication at the same time every day. You will record the number of study medication doses that you gave to your child in a diary. When your child has completed the study, you will return the unfinished medication bottles and the medication diary to us in a postage-paid box that we will provide for you. Dexamethasone is approved by the FDA for use in children to treat local inflammation (for example, in asthma and croup), but not specifically to prevent inflammation or scarring in the kidney.



What will happen at today's visit?

Today we will:

- Ask about your child's medical history including:
 - family history of UTI and kidney disease
 - medications
 - date of birth
 - contact information
- Collect about 2 teaspoons (11.5 mL) of urine to check for signs of infection in the kidney. If there is extra urine from the sample that your child's doctor collected, we will use that. If there is not enough urine, your child can urinate in a cup or a bag. E. coli is the germ that causes most UTIs. Some E. coli can stick to the lining of the urinary tract which makes it easier to cause an infection. We will do genetic testing on the germ to identify the different kinds of E. coli.
- Collect about 1 teaspoon (6 mL) of blood to check for signs of infection in the kidney. If you are reluctant to have your child's blood drawn, you may choose not to have this done.
- Ask you to complete questionnaires about your child's urination and bowel movements.

Consent for blood draw:

Yes Initials _____

No Initials _____

If you agree, we would like to collect an additional teaspoon (3mL) of blood to look at DNA (heredity material with information about the structure and function of cells) to decide which children have a greater chance of developing scarring in the kidney after a UTI. This sample can be collected during today's visit or at the time of your child's DMSA scan. You will not be informed of the results of the genetic testing of this sample because at this time we don't know how this information would be helpful. The DNA that your child provides as a participant in this research study will be considered a donation. You and your child will not have any property rights to the samples, nor will you and your child have any property rights to or be entitled to compensation of any type for products, data, or other items or information that is developed from the samples. The samples will be assigned a code number and the information linking the code with your child's identity will be stored in a separate secure location. Your child's samples may be shared without identifiers with other investigators. Some of the blood and urine will be stored at the University of Pittsburgh for future studies about urinary tract infections.

Consent for genetic sample banking:

Yes Initials _____

No Initials _____

All samples will be stored indefinitely. The standard urine tests ordered by your child's doctor to look for a urinary tract infection, such as the urine culture, will be charged to your child's insurance. The specialized testing of the bacteria, the urine and the blood as described, will be paid for by the study. This visit will take place at the location where your child was diagnosed with the UTI. It will take about 1 hour.

Follow-up phone call

We will call you for the next 3 days. If your child's fever has not resolved by day 4, we will continue daily phone calls until your child's fever resolves. If the urine culture that your doctor sent to the lab is negative your child cannot stay in the study. You will be instructed to stop the study medication and a DMSA scan will not be performed. You should follow-up with your child's primary care provider as directed.

If the urine culture that your doctor sent is positive, your child can stay in the study. We will call you once a month for the next 6 months to find out how your child is doing. **If your child has a fever or signs of a urinary tract infection, we will see your child right away** and collect urine to figure out if your child is having another UTI. Please call 412-996-2653 for an appointment. If your child is having a second



infection, we will treat your child with the same medication (either steroids or placebo) that was used for the first infection along with appropriate antibiotics. This treatment will be started as soon as possible after your child is diagnosed with a UTI (but no later than 48 hours of starting antibiotic therapy). The dose of study medicine will depend on your child's weight (0.15 mg per dose for every 2.2 pounds that your child weighs). Your child will take the study medication or placebo (0.15 mg/kg per dose) twice a day for 3 days. You will be asked to give the medication at the same time every day with a meal to reduce the risk of stomach aches. We will also ask you to give the dose of medication again if vomiting occurs within 20 minutes of giving the initial dose of medication. We will communicate with your primary care provider about your child's infection and treatment.

Your child will have a DMSA (Dimercaptosuccinic acid) kidney scan in approximately 6 months after the initial UTI to see if there is inflammation or scarring in the kidney. If your child has more than one UTI, the scan will be done 4 months after the last UTI. A DMSA scan is a test that can look at the shape of the kidneys and evaluate how much scarring is present. Your child will have a small amount of technetium-99m (a radioactive chemical), injected into a vein of the arm or hand. After the injection, you will be able to leave the radiology department and then return in approximately 1.5 to 3 hours after the injection. This delay will allow the kidneys to absorb the DMSA. When you return, we will ask your child to urinate and then we can obtain the pictures of the kidney. Your child can sleep during this part of the test. The imaging will take about 30-60 minutes. Your child's doctor will receive the test results. To prepare you and your child for the scan, the study nurse will give you printed information about the kidney scan. This scan is commonly done after a UTI and will be paid for by the study. The scan is done at Children's Hospital in Lawrenceville.

What are the possible risks, side effects and discomforts of this research study?

As with any research study, there may be adverse events or side effects that are currently unknown, and it is possible that these unknown risks could be permanent or serious.

DMSA scan: A DMSA kidney scan is used to show areas of kidney infection or kidney damage. A DMSA scan requires inserting an intravenous (IV), injecting a radioactive substance into the blood stream, and taking a picture of the kidneys with a special camera. Frequently, children may have some discomfort with the placement of the IV. IVs can fall out and some fluid can go into the arm outside of the vein, but this is rare. Participation in this research study involves exposure to radiation from a DMSA scan. The amount of radiation exposure that your child will receive from this procedure is approximately 0.14 rem (a unit of radiation exposure) to your child's kidneys, with minimal exposure to other body areas. For comparison, radiation workers are permitted, by federal regulation, a maximum annual radiation exposure of 20 rems to the most sensitive organs of their body. Also, the radiation exposure from a DMSA scan is less than half of the natural background radiation during one year. There is no known minimum level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects (abnormal cells) or cancer. However, the risk associated with the amount of radiation exposure that your child will receive from this study is considered to be low and comparable to everyday risks.

Steroid Treatment: Because your child will be getting a small dose for only 3 days of steroid (about the same dose that is used for asthma) the risk of side effects is low. Side effects from steroids may include increased appetite, increased activity level, increased blood pressure, allergic reaction including skin rash, high blood sugar, stomach ulcers or bleeding, thrush (yeast infection of the mouth), temporary white blood cell increase, depressed mood, insomnia, worsened glaucoma, and increased risk of infections.

Loss of Confidentiality: There is a rare risk of the loss of confidentiality. The study staff are trained and experienced in protecting health information (date of birth, medical record number, or names) as confidential information. Subjects will be identified only by a study number on the forms that are kept safe in a locked cabinet or in locked computer databases protected by password and firewall. Only the study staff will have passwords to the computers in secure offices.



Blood draws: Blood draws may cause mild pain, bleeding, or bruising. Fainting and infection are rare complications. To protect children, all blood draws will be performed by qualified nurses, physicians and phlebotomists (healthcare workers trained in drawing blood for analysis or transfusion) according to standard techniques.

Topical Anesthetic Lidocaine (cream to decrease pain with blood draw) will be available as an option to use before the blood is drawn. There is a risk of slight skin irritation when using this cream.

Genetic Testing: Any results of the search for genes that could increase risk of kidney scarring are preliminary and would require more studies to understand how to use this knowledge. Not knowing the results could cause distress for some parents. The genetic tests will be limited to questions regarding urinary tract infections. The samples will be stored without identifiers.

Urine Sample: If your child is toilet-trained, the urine sample can be collected in a cup which may cause your child to feel some anxiety. If your child is not toilet trained, we will collect the sample with a small catheter. The catheter may cause some discomfort; being restrained briefly may be upsetting for your child. To decrease the chance of discomfort, a trained registered nurse will obtain the sample. Sometimes, a urine bag may be applied to catch the urine, but if the sample tests positive for infection, we will obtain a sample with a catheter.

What are the possible benefits of this study?

There may be direct benefit from this study for your child and information discovered may improve the care of children with UTI in the future. Steroids may or may not decrease your child's chance of developing kidney scarring.

What treatments or procedures are available for my child if I decide not to take part in this study?

You may choose not to have your child participate in this study. Alternatives to your child's participation include taking antibiotics alone (without steroids).

Will we be told of any new risks that may be found during the course of the study?

You will be promptly notified if any new information regarding new risks develops during the course of this study which may cause you to change your mind about having your child continue to participate.

Will our insurance be charged for costs of any procedures in the study?

You and/or your insurer will be billed for any routine care services that are provided. You will be responsible for any applicable co-pays, coinsurances, and deductibles. You will be responsible for your child's initial antibiotic prescription for the UTI. There will be no costs to you or your insurance company for the study visit today. The cost of the study medication (steroid/placebo), all urine and blood tests and the DMSA kidney scan will be covered by the study.

Will my child be paid for participating in the study?

To help cover travel expenses you will be given \$25 today and a parking pass while you are here for the visit. You will also receive \$75 when your child has the DMSA kidney scan.

Who will pay if my child is injured as a result of this study?

If you believe that the research procedures have resulted in an injury to your child, immediately contact the Principal Investigator who is listed on the first page of this form.

Emergency medical treatment for injuries solely and directly related to your child's participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your child's research-related injury requires medical care beyond this emergency treatment, you will be



responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

Who will know about my child's participation in this research study?

Any identifiable information about your child obtained from this research will be kept as confidential (private) as possible. All records related to your child's involvement in this research study will be stored in a locked file cabinet. Your child's identity on these records will be indicated by a case number rather than by name, and the information linking these case numbers with the identity will be kept separate from the research records. Your child will not be identified by name in any publication of the research results.

Will this research study involve the use or disclosure of my child's identifiable medical information?

This research study will involve the recording of past, current and/or future identifiable medical information from your child's hospital and/or other health care provider (e.g., physician office) records. The recorded information will be limited to the results of any laboratory tests, diagnostic tests, side effects related to the study and/or illnesses.

We will take measures to protect your child's privacy, although no guarantee of confidentiality can be absolute. Before your child's sample is sent to the labs, the sample will be labeled with the study identification number. Personal identifying information such as name, address, and date of birth will be removed. The lab may have some data about your child such as age, sex, race, and diagnosis. You will not be given any information, nor will any information appear in your child's medical record, as to how these samples are used.

The results of the DMSA kidney scan will be placed into your child's medical record and shared with your child's primary care provider. The results of the genetic tests or inflammatory markers will not be put into your child's medical records.

Who will have access to identifiable information related to my child's participation in this study?

In addition to the investigators listed on the first page of this consent form and their research staff, the following individuals may have access to identifiable information related to your child's participation in this research study.

- Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your child's identifiable research information (which may include your child's identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study. In unusual cases, the investigators may be required to release identifiable information (which may include your child's identifiable medical information) related to your child's participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies. Research investigators may be required under Pennsylvania law to report any suspicion of child abuse to child protection services. If the investigators learn that you or someone with whom you are involved is in serious danger or potential severe harm, they may need to warn those who are in danger and contact other agencies to ensure safety.
- Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your child's identifiable medical information) related to your child's participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g. laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct



payment for tests and procedures ordered by the investigators; and/or (3) assessing internal hospital operations (i.e. quality assurance).

- Authorized representatives of the NIH, the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) may review and/or obtain your child's identifiable medical information for the purpose of monitoring the accuracy and completeness of the research data, for performing required scientific analyses of the research, and re-analyses of the research data at a later date and to be sure that the research is being conducted according to the guidelines of each institution. While these organizations have provided their assurance that they will not release your child's identifiable medical information to anyone else, the Children's Hospital of Pittsburgh cannot guarantee this. In unusual cases, the investigators may be required to release your child's research information in response to a court order.
- Two radiologists at Children's National Hospital, Washington, DC will review all DMSA kidney scans.

How long will the investigators be permitted to use and share identifiable information related to my child's participation in this study?

Dr. Shaikh and his study staff will be permitted to use your child's identifiable health information indefinitely. In addition, they will contact you a few months after you finish the study to share information about the study findings and to discuss other UTI research opportunities that you might find of interest.

May I have access to the medical information that results from my child's participation in this study?

In accordance with the Children's Hospital of Pittsburgh of UPMC Notice of Privacy Practices document which you have been provided, you are allowed to look at information (including information resulting from your child's participation in this research study) contained within your child's medical records unless specifically stated. In this, study, the researcher or you will not know which medicine your child is taking (active or placebo medication). After the study is finished and the results have been studied, we will send you a letter that tells you which medication your child received.

Is my child's participation in this study voluntary?

Your child's participation in this research study will include the use and sharing of identifiable information for the purposes described above and is completely voluntary. If you do not provide your consent, your child will not be allowed to participate in the research study. Your decision regarding your child's participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh or medical care at a UPMC hospital or affiliated health care provider or relationship with a health care insurance provider.

Your child's doctor may be involved as an investigator in this research study. As both your child's doctor and a research investigator, s/he is interested both in your child's medical care and the conduct of this research study. Before agreeing to participate in this research study or at any time during your study participation, you may discuss your child's care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

May I withdraw my consent for my child's participation in this study at a future date?

Yes, you may withdraw your consent for your child's participation. The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your child's identifiable medical information) related to your child's participation in this research study. This information will be maintained indefinitely. Because your child's samples are retained indefinitely they will



continue to be used in the event that your child is withdrawn from the study.

Can my child be removed from the study without my consent?

The researchers also have the right to stop your child's participation if your child has had an unexpected reaction, you have failed to follow instructions, other reasons that the investigator is concerned about your child or because the entire study has been stopped.



Voluntary Consent and Authorization

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that have occurred during my participation. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me.

Printed Name of Child (Research Subject)

I understand that, as a minor (age less than 18 years), the above-named child is not permitted to participate in this research study without my consent. Therefore, by signing this form, I give my consent for his/her participation in this research study and allow the use and sharing of my child's medical record information for the purposes described above.

Printed Name of Parent

Relationship to Child

Signature of Parent

Date

Certification of Informed Consent

I certify that I have explained the nature and purpose of this research study to the above-named individual and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about the study have been answered and we will always be available to address future questions as they arise. I further certify that no component of this protocol was begun until after this consent form was signed.

Printed Name of Person Obtaining Consent

Role in Research Study

Signature of Investigator

Date

