Informed Consent Cover Page for FDAAA consent posting:

Official Title:	Best Noninvasive Predictor of Renal Function in Assessing Adult Sickle Nephropathy
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PRINCIPAL INVESTIGATOR: Emily Limerick, M.D.

STUDY TITLE: Best Noninvasive Predictor of Renal Function in Assessing Adult Sickle Nephropathy

STUDY SITE: NIH Clinical Center

Cohort: *Standard*

Consent Version: 02/21/2020

WHO DO I CONTACT ABOUT THIS STUDY?

Principal Investigator, Emily Limerick, M.D.; Building 10-CRC, Room 6N-254, Telephone: 301-480-4241; E-mail: emily.limerick@nih.gov

Study Coordinator, Julia Varga, RN; Building 10-CRC, Room 5E-1424 Telephone: 301-402-35951; E-mail: julia.varga@nih.gov

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you to in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

The goal of this research study is to determine which of two different lab tests is the best to measure kidney function in adults with sickle cell disease. This is an important question to answer because kidney disease is a major cause of problems in patients with sickle cell disease. Using the most accurate test to check kidney function is important to identify issues earlier so we start treatment when appropriate and may be able to stop the progression of kidney disease.

There are data to suggest that for sickle cell patients, a blood test called cystatin C is a better marker of kidney problems, better than the most commonly used creatinine test. Therefore, we will measure both of these levels and compare to a 'gold standard', the iothalamate test, where a small amount of iodine-based radiocontrast material is used to evaluate the health of your kidneys. We will also measure other markers of kidney function in both the blood and urine to see how they compare to the iothalamate test. Most studies compare *estimates* of kidney function, but this research will use the iothalamate test to *directly measure* kidney function and help determine the best way to evaluate for kidney disease in SCD.

Participation in this research is voluntary. Study participants should be adults with sickle cell disease who are interested in helping other sickle cell patients; this research may not directly impact study participants. This research requires multiple visits to the NIH over the course of

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several weeks. While in the study, participants will have multiple blood draws, receive an injection of a material to check kidney function (iothalamate), provide a 24-hour urine collection, and undergo a kidney MRI. One test to check kidney function requires participants return to the NIH two days in a row and have several timed blood draws.

The main risk is a potential reaction to the iodine-based injection material used in measuring kidney function; such reactions are rare but may be severe so patients at increased risk are excluded from the study. Participants will be paid for their time. Study participation will not impact clinical care or access to other treatments.

The remaining document will now describe more about the research study and should also be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY THIS STUDY IS BEING DONE?

This is a research study about kidney problems in sickle cell disease (SCD). We hope that the results of this study will help us understand more about how to assess for kidney disease in sickle cell patients. The most common tests that we currently use to assess for kidney damage in sickle cell patients often underestimates how much kidney damage that has occurred; which means we may not know a patient has chronic kidney disease until it has already caused significant injury. Better testing is important to allow earlier detection of kidney disease. There are data to suggest that for sickle cell patients, a blood test called cystatin C is a better marker of kidney problems, better than the most commonly used creatinine test. Therefore, we will measure both of these levels and compare to a 'gold standard', the iothalamate test, where a small amount of iodine-based radiocontrast material is used to evaluate the health of your kidneys. We will also test other new strategies for evaluating kidney injury which have not been fully evaluated in sickle cell disease, including blood and urine tests as well as non-contrast kidney MRI.

WHAT WILL HAPPEN DURING THE STUDY?

If you decide to take part in this study, you will be asked to come to the Clinical Center of the National Institutes of Health where you will be evaluated. The following tests will be done on multiple days:

Study Procedures				
Screening		**Visit 1**	**Visit 2**	***Visit 3***
Eligible patients will sign consent at their initial screening visit	**24 HOUR URINE COLLECTION**	1. Return urine sample 2. Heigh/weight and vital signs 3. Blood collection and iothalamate test	1. Vital signs/BP 2. Final iothalamate blood draw 3. Kidney MRI	*1. Vital signs/BP* *2. Kidney MRI if not completed at prior visit*

Screening

A member of the study team will tell you about the study and ask you some questions to determine if you are eligible for this study. We will take up to 6 tablespoons of blood from a vein in your arm using a needle. The amount of blood drawn is considered a safe amount for adults per NIH guidelines. We will use your blood to confirm you have sickle cell disease and ensure you meet the list of participation criteria listed above. We will also use your blood to run some standard clinical labs.

First Visit (Iothalamate test)

At your first study visit you will have up to 6 tablespoons of blood taken. As part of the study, you will collect your urine for 24 hours and bring the completed urine sample to this visit. The iothalamate test will be performed at this visit. You will have your blood pressure and vitals measured at each study visit.

Second Visit (Kidney MRI)

At your second visit you will have up to 6 tablespoons of blood taken to complete the iothalamate test. The kidney MRI test will be performed at this visit.

You may have to complete a third study visit for the kidney MRI test if we are unable to schedule it the same day as the second visit.

*Note: all study visits must be completed within 8 weeks of study enrollment.

24-hour urine collection

This test is done to check kidney function. It is done by collecting your urine in a special container(s) over a full 24-hour period. The container must be kept cool until the urine is returned to the NIH. The team will provide you with the containers to collect and store the urine. It is important to collect all the urine voided in a 24-hour period so, if possible, choose a day when you will be at home so you do not have to transport your urine.

Research Procedures:

Screening:

After you agree to be in the study and sign this consent form, we will do the following:

Iothalamate test: we will insert a peripheral IV, a small catheter, into your vein. The catheter will remain in place for the duration of the iothalamate test to allow injection of radiocontrast material. We will collect blood prior to the start of the test. When the test begins a special contrast agent will be injected through the IV; we will then collect your blood at five different time points over the next 4 hours. The IV allows for repeated blood collection without the need for repeated needle sticks. The amount of blood drawn is considered a safe amount for adults. You will need to return the day after the iothalamate injection for a final blood draw about 24 hours after the initial injection. We will plan for a kidney MRI to be performed that day as well.

Blood Collection: As described above, we will take blood from a vein in your arm using a needle. The amount of blood drawn is considered a safe amount for adults per NIH guidelines. We will use your blood to run some standard clinical labs, to measure the kidney function markers we are studying in this clinical protocol as well as to measure your kidney function during the iothalamate test.

24-hour urine collection: we will provide you with the necessary equipment to be able to collect all of your urine at home over the course of a 24-hour period. You will bring that sample back to the NIH Clinical Center for testing, to include routine clinical tests as well as special testing of certain proteins in your urine.

Kidney MRI: MRI will be performed; during the test you will be asked to lie down on a movable table that slides into a long narrow tube. The MRI may last for up to an hour; you must hold very still during this procedure. Participants who are unable to complete MRI are still eligible for study participation and will complete other study elements.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last between 3 to 8 weeks with 2 or 3 visits to the NIH Clinical Center. You will come in for a screening visit at which we will decide if you are eligible to participate in this study.

Your participation in this study will end after you have completed all the study procedures. Participants may be asked for permission to call them back to discuss additional studies and obtain consent if they are eligible and interested in participating.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have up to 70 individuals with sickle cell disease who may participate in this study at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

a) **IV placement/Blood collection**: There may be some discomfort on your arm when we insert an IV and/or collect your blood with a needle. There is a small chance that you will get a bruise, feel lightheaded, faint, or have an infection at the place where you were pricked. There is a risk that multiple IV placement attempts may be required to successfully secure the catheter for use throughout the iothalamate test.

b) **Iothalamate test:** Participants will undergo an iothalamate test, which may result in possible reactions to the radiographic contrast agent. Reactions may be mild and include nausea, vomiting, flushing, or feelings of warmth; rarely more severe reactions may occur such as hives, breathing difficulties, and anaphylaxis. This is why patients with allergy to iodine products will be excluded from study participation. Participants with a history of nausea or vomiting following administration of these iodine products will not be excluded since these symptoms do not correlate with increased risk of severe allergic reactions.

c) **MRI without contrast:** MRI uses no harmful radiation and is generally safe. MRIs do pose a potential risk for patients with implanted metal objects (i.e. cerebral aneurysm clips, cochlear implants, etc.). The magnetic field can cause twisting or movement of these objects which can harm patients. Also, the MRI can potentially cause burns in patients with pacemakers or other internal wires. Patients will be screened for these types of risks and will not undergo MRI if these objects could cause problems with the MRI. Patients who are not willing or not able to undergo MRI can still be enrolled on to this protocol.

The MRI may rarely cause discomfort from nerve stimulation. Typically, patients may feel a twitch such as in the buttock, leg, or across the bridge of the nose. There is no physical danger from nerve stimulation. The MRI technician will use settings to minimize the potential for pain.

The MRI also generates noise in the scanner. All subjects will wear earplugs and/or headphones to protect hearing.

There are some known minor adverse effects of the MRI, these may include nausea, metallic taste, and seeing of flashes of light. To avoid these, the subjects will be asked to walk slowly to the patient table and the table will be moved slowly into the magnet.

d) **Publication:** We may publish results of this research study in scientific journals and public databases, including your medical history and other medical information but the information provided in the publications will be anonymous. It is possible but unlikely that you and/or a family member could be identified because of such publications.

What are the risks related to pregnancy?

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. You must tell the study doctor if your birth control method fails while you are in the study. If you think or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the course of this study drug or procedures on this study.

You may not participate in this study if you are pregnant. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

What are the risks of radiation from research?

MRI without contrast: MRI uses no ionizing radiation and is generally safe when performed on a properly screened population.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You will not benefit from being in this study.

Are there any potential benefits to others that might result from research?

In the future, other people might benefit from this study because we will understand better how to monitor for kidney problems in sickle cell patients. This study could help us to find kidney problems earlier than our current methods and potentially prevent worsening kidney disease.

WHAT OTHER OPTIONS ARE THERE FOR ME?

You do not have to participate in this study if you do not want to. You may withdraw from this study at any time. If you decide to withdraw from the study, we would like to keep your test results to properly analyze this research study. If you have concerns about this, please speak with members of your research team.

This study does not investigate new treatments and will not affect your current treatment regimen.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

Results of research tests will not be made available during the study. If you would like the results of the standard clinical labs please contact a member of your research team.

EARLY WITHDRAWAL FROM THE STUDY

Discontinuing Participation: If you decide to stop participating in this study, you may request this by either informing the investigators or by writing to the research team to the address at the end of this consent (under Problems and Questions on last page of consent). You will not be asked for further information or samples.

Research Subject's Rights: You are free to refuse to undergo any of these tests. You may withdraw from the study at any time. If you decide to participate and later change your mind, you are free to stop participation at any time. You will not be penalized or lose benefits to which you are otherwise entitled. Refusal to participate will not affect your legal rights or the quality of health care that you may receive at this center.

Explanation of Conditions for Early Withdrawal: If new previously undisclosed information emerges during the study that would exclude you from the study, the investigators looking after you will discuss these with you.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Food and Drug Administration (FDA) and the Office for Human Research Protections, which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

This study is protected by a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances. Please refer to the OTHER IMPORTANT INFORMATION section near the end of this consent form for more information on this type of protection.

WILL YOU SAVE MY SAMPLES OR DATA FOR USE IN OTHER RESEARCH STUDIES?

As part of this study, we are obtaining blood and urine from you. We plan to use specimens and data for studies going on right now, as well as studies in the future. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. Samples provided to outside institutions will be sent without any personal identifying information, meaning these samples could never be traced back to you. However, the code will be linked through a key to information that can identify you. These studies may provide additional information that will be helpful in understanding Sickle Cell Disease, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial_partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

As part of this study, some of your information will be placed into your electronic health record maintained by the NIH. These data may be used for future research studies by NIH researchers without contacting you to ask for your permission. Because this information is part of your medical record, even if you say "NO" to the questions below on future use and sharing, we cannot always remove this information from your health record or prevent its future use for research. However, in most circumstances, any identifying information about you will be removed from your data before it is used by other researchers.

If you change your mind and do not want us to store and use your data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your samples. For example, if some research with your blood/urine/data has already been completed, the information from that research may still be used. Also, for example, if the blood/urine/data has been shared already with other researchers, it might not be possible to withdraw the blood/urine/data.

Please place your initials in the blank next to Yes or No for each of the questions below:

My specimens and data may be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

My specimens and data may be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

How Long Will My Samples and Data be Stored by the NIH?

Your blood and urine samples may be stored at NIH indefinitely.

Risks of Storage and Sharing of Samples and Data

When we store your data and/or samples, we take precautions to protect your information from others that should not have access to it. When we share your data and/or samples, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your data or samples.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will I receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation is guided by NIH policies and guidelines.

You will receive compensation to cover time and inconvenience for the routine diagnostic and research tests. The compensation amount will be dependent on the research tests performed. You may receive up to $500 for your participation in this study: $350 for completion of study procedures as well as an additional $150 for successful completion of all study visits and procedures. If you are unable to complete all aspects of the study, you will receive compensation for the research procedures you finish prior to study withdrawal.

Research Procedures	Inconvenience Units	Compensation per procedure	Frequency	Total Compensation
Medical History and Physical Examination	2.5	$25.00	1	$25.00
Outpatient Visits (first hour)	2	$20.00	3	$60.00
Outpatient Visits (additional hours up to 4 hours)	1	$10.00	9	$90.00
Screening Blood Draw	1	$10.00	1	$10.00
Urinalysis/Urine Sample	1	$10.00	1	$10.00
24-Hour Urine Collection	2.5	$25.00	1	$25.00
IV placement	1	$10.00	1	$10.00
Radiocontrast Infusion/ Administration by IV	5	$50	1	$50
Serial IV Sampling	1	$10	1	$10
24-hr Iothalamate Blood Draw (visit 2)	1	$10.00	1	$10.00
Kidney MRI	5	$50	1	$50
Completion of all study visits and procedures				$150
Maximum Compensation:				$500.00

The NIH has guidelines for the participation of its staff in research protocols. If you are a NIH staff member, please refer to the NIH Manual Chapter 2300-630-3 which details the NIH leave policy for NIH employees who participate in NIH protocols. Participants who NIH staff members are should be aware of these guidelines and discuss any questions they have with the research team.

If you are unable to finish the study, you will receive compensation for the specific procedures you completed (see table above) prior to discontinuation.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Review Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will I receive reimbursement or direct payment by NIH as part of my participation?

This study does not provide reimbursement or payment for travel, lodging or meals while participating in the research.

Will taking part in this research study cost me anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- You will undergo study procedures at no charge to you. This may include medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH). Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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. At most, the Web site will include a summary of the results. You can search this Web site at any time.

OTHER IMPORTANT INFORMATION

Confidentiality

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the

insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove any information that shows your identity before sharing them. You should be aware that there is a slight possibility that someone could figure out the information is about you.

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). NIH researchers must use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. NIH researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

There are several circumstances in which the Certificate does not provide protection. These include when information:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is necessary for your medical treatment and you have consented to this disclosure;
4. is for other research;
5. is disclosed with your consent

In addition, identifiable, sensitive information collected or compiled during research and protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent. You should understand that a Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, medical care provider, or other person obtains your written consent for us to disclose the research information, then the researchers will not use the Certificate to withhold that information.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures.

The protections of the Certificate apply to all copies of the identifiable, sensitive information collected or compiled during the research. Therefore, if an NIH investigator shares a copy of your identifiable, sensitive information with any other investigator or institution (whether a collaborator on this study, or researcher conducting secondary research in the future) that party must generally agree to comply with the disclosure restrictions under the Certificate described above.

Additionally, the Federal Privacy Act generally protects the confidentiality of your NIH medical records. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. However,

NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

Policy Regarding Research-Related Injuries

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

Problems or Questions

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Emily Limerick, MD; emily.limerick@nih.gov, 301-480-4241. *Other researchers you may call are:* Julia Varga, RN; Telephone: 301-402-3595. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

Consent Document

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process with a non-English speaking subject and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.