STUDY TITLE: PRE-EMPTIVE GENOTYPING OF CHILDREN AND ADOLESCENTS AT RISK FOR SURGERY AND SUBSEQUENT PAIN MANAGEMENT

STUDY NUMBER: 2013-0853

FUNDING ORGANIZATION: The National Institutes of Health and the Department of Anesthesia.

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INTRODUCTION

We are asking for your permission for you to be in a research study so that we can learn new information that may help others. If you decide not to give your permission for you to be in this study, we will still take good care of you. If you decide to be in this study, you may change your mind at any time during the study and you can stop being in the study. Take all the time you need to make your choice. Ask us any questions you have. It is also okay to ask more questions after you decide to be in the study. You can ask questions at any time.

WHY ARE WE DOING THIS RESEARCH?

In this research study, we want to learn about the safety and usefulness of genetic testing before surgery to predict your response to pain medicines. Pain medicines affect people differently. We believe genes are responsible for some of those differences. Testing genes before a person needs pain medicine is called pre-emptive genetic testing. We expect that placing results from pre-emptive testing in the electronic medical record could help doctors make decisions about the best pain medicine and best dose for you after surgery. We expect this will increase the chances that pain medicine will help. We also expect this will lower the chances of side effects. We are asking you and others who are being seen in clinic for possible surgery to be in a research study. Oxycodone is a pain medicine given in pill or liquid form after many surgeries. The pre-emptive genetic test will give doctors suggestions about how best to use oxycodone as well as codeine, hydrocodone, and tramadol. We believe genetic testing will improve how pain medicines work when people are healing after surgery. We hope this study will improve clinical practices.

WHO IS IN CHARGE OF THE RESEARCH?

Senthilkumar Sadhasivam, MD, MPH is the researcher at Cincinnati Children's Hospital Medical Center (CCHMC) that is in charge of this study.

CCHMC is being funded by the National Institutes of Health and the Department of Anesthesia, to do this study.

WHO SHOULD NOT BE IN THE STUDY?

You cannot be in this study if you:

1. Are younger than 2 or are 22 years old or older
2. Have significant comorbidities (ASA 4 and 5)
3. Have liver or kidney failure
4. Have a neurodegenerative disease
5. Have a severe pulmonary disease (e.g. cystic fibrosis)
6. Are known to have a substance abuse problem
7. Are taking other medicines that affect how well certain pain medicines work. Be sure to ask the study doctors about this if you are taking any medicines.

WHAT WILL HAPPEN IN THE STUDY?

The research staff will explain the study to you and you will be able to ask questions to make sure that you understand what it is involved in the study.

If you can be in the study and you decide to be in the study, you will be asked to come in for up to two study visits. While in the study, you will be asked to do the following:

1. The first visit (in person or by the phone) is to explain the details of the study. If you give us permission, we will collect a blood sample for DNA and test your genes. If you are afraid of needles, we will collect a spit sample from you. At this time, you will be given a study I.D number to keep your study information a secret to study team members. If your genetic test result is placed in your medical record as part of the study, the result will be linked to your name and medical record number. If we do not get enough DNA from your sample, we may need to ask you for another sample.
2. After we receive your sample and test the genes, we may or may not place your results into your medical records.
3. The second visit will happen if you need to have inpatient surgery. While you are in the hospital, we will ask you to fill out a one page Pain Medicine Report. This report must be completed at least 24 hours after you are given pain medicines only in pill or liquid form. If study staff cannot collect your completed report on day of discharge, a staff member may call you to complete the report by phone.
4. If you require a surgery that is outpatient, such as a tonsillectomy or wisdom teeth removal, you will fill out a home pain diary. You will record your pain levels using a 0-100 scale beginning on the evening of the surgery date to the end of the second day after surgery. During the same time you will also record the amount and quality of sleep you get, your daily food intake, and any problems that may arise due to the medicine.

5. Throughout the study, the study team will collect information from your medical records for the study.

You may be placed in one of two groups. We are starting the study by placing everyone in the same group. Everyone in the first part of the study will have their genetic test results placed in their medical records. People who join the study during the second part of the study will be placed in one of two groups. This will be done by randomization, which is a way of choosing by chance, like flipping a coin. One group will have genetic test results placed in their medical records. If people in this group need surgery, we will learn how their doctors use the results to pick pain medicine after surgery. We will learn if people in this group have lower pain and less side effects when doctors use these results. The second group will also have DNA taken from blood or spit during the first study visit. It may take up to 3 years for this group's genes to be tested. The genetic test results will not be placed in the medical record during the study period. If you need surgery, the doctors will use standard practice for choosing pain medicines. Your doctors can order the genetic test if they think it will be helpful when you have surgery. You will not know what group you are in.

The study will last for 6 years, however, researchers may spend an additional 2 years analyzing data and publishing the results.

By signing this form, you are giving permission for us to store your sample and data for future research in human health.

WHAT ARE THE GOOD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

Participating in the study may not directly help you right now. However, children or young adults whose genetic results are placed in the medical records may benefit by better pain management.

WHAT ARE THE BAD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

- If blood is drawn, you may feel brief pain from the needle. You may have some bruising or swelling. Infection, light-headedness and fainting are also possible but unlikely.
- Travel and time required for the visits may be inconvenient.
- What we understand about genetic test results may change as more studies are done. This may cause confusion, emotional distress, or possible clinical, behavioral, and economical consequences.
- Your identity may be accidently discovered even though we try our best to keep the information private.
- Your insurance company may find out about your genetic test results if we place them in your medical record as a part of this study.
- There may be unknown or unforeseen risks associated with the study participation.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this study, you can choose not to be in it.

HOW WILL YOUR INFORMATION BE KEPT PRIVATE?

Making sure that your information remains private is important to us. To protect your privacy in this research study we will:

- Use a study ID number unique for you. The study ID number will be used for study forms and electronic data storage.
- Keep your study number secret so that only study staff will know it.
- Use a barcode for the DNA sample that is unique to you when we store the DNA. We will also use a barcode when we send a portion of your DNA to a laboratory outside of CCHMC for genetic testing that is needed for this study. The barcodes will be the only way to identify the DNA samples came from you. The barcode numbers linked to your study number will be maintained in a password protected file in a secured network drive.
- Use a study ID number to identify your demographic and clinical data. This will be maintained in a password protected file on a secured hospital network.
- Keep your paper study records and data in a locked office or file within the Department of Anesthesiology or The Center for Autoimmune Genomics and Etiology.

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

CERTIFICATE OF CONFIDENTIALITY

We will do everything we can to keep others from learning about your child's participation in this study. To further help protect your child's privacy, we have obtained a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS).

With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify your child in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify your child, except to prevent serious harm to your child or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, your child, or your involvement in this study.

A Certificate of Confidentiality cannot be used to refuse to disclose identifiable research information about a minor if a parent or legal guardian requests it. The researchers may use other basis for a refusal to disclose information after checking with their IRB about waivers of parental permission and other issues.

If an insurer or employer learns about your or your child's participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Disclosure will be necessary, however, upon request from personnel of the United States federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that we will in all cases, take the necessary action, including reporting to authorities, to prevent serious harm to yourself, children, or others. For example, in the case of child abuse or neglect researcher will take necessary actions to protect the child.

WHAT IF WE LEARN NEW INFORMATION DURING THE RESEARCH?

The study doctor will tell you if they find out about new information from this or other studies that may affect your health, safety or your willingness for you to stay in this study.

WILL IT COST YOU ANYTHING EXTRA FOR YOU TO BE IN THE RESEARCH STUDY?

Your insurance company will be billed for usual costs of your medical care, but **will not** and **should not** be charged for participation in the study. Tests done specifically for the study will be paid for by the study.

WILL YOU BE PAID TO BE IN THIS RESEARCH STUDY?

You will be reimbursed for your time and effort while you are in this research study.

If you need surgery, you will receive $20 after completing the study survey or returning the completed diary.

Reimbursement for participating will be paid on the following schedule:
$20 for completing visit 2

We will give you your payment in the form of a reloadable debit card (Clincard) and you will receive a handout that will explain how to use the card. We will provide you with a card and we will load money onto your card after each visit that you complete based on the schedule listed above.

Because this research study involves payment for participation, we are required by Internal Revenue Service (IRS) rules to collect and use your social security number (SSN) or taxpayer identification number (TIN) in order to track the amount of money that we pay you. Unless you have given specific permission for another use of your SSN or TIN related to this research study, we will only use your SSN or TIN to keep track of how much money we pay you and your SSN or TIN will not be used as part of this research study.

WHAT HAPPENS IF YOU ARE INJURED FROM BEING IN THIS STUDY?

If you believe that you have been injured as a result of this research you should contact Senthilkumar Sadhasivam as soon as possible to discuss the concerns. Treatment for injuries is available at

CCHMC. If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in a research study. If possible, you should give them a copy of this permission form.

CCHMC follows a policy of making all decisions about compensation for the medical treatment of physical injuries that happened during or were caused by research on an individual basis.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

For questions, concerns, or complaints about this research study you can contact the study staff listed on page 1.

If you would like to talk to someone that is not part of the research staff or if you have general questions about your research study rights or questions, concerns, or complaints about the research, you can call the CCHMC Institutional Review Board at 513-636-8039.

WHAT ELSE SHOULD YOU KNOW ABOUT THE RESEARCH?

During the study period, researchers may find changed genes different from the ones we are interested in as part of this study (called incidental findings). If experts believe the incidental findings are important to your health, we want to contact you. The study member who contacts you will ask you if you want to learn the results. If you say yes, the results will be explained during a genetic counseling visit or will be given to your doctor. Your insurance will be billed for a genetic counseling visit. Any incidental results we tell you about will be placed in your medical record.
Is this ok? _____ (initial) Yes -or- _____ (initial) No

As a part of this study, your de-identified data and sample may be shared with other researchers or data warehouses for studies in human health.

Do you want to be re-contacted in the future about other studies you might be able to participate in?
_____ (initial) Yes -or- _____ (initial) No

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your “protected health information” (called PHI for short).

What protected health information will be used and shared during this study?
CCHMC will need to use and share your PHI as part of this study. This PHI will come from:
- Your CCHMC medical records
- Your research records

The types of information that will be used and shared from these records include:
- Laboratory test results, diagnosis, and medicines
- Reports and notes from clinical and research observations

- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- If applicable, information concerning HIV testing or the treatment of AIDS or AIDS-related conditions, drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

Who will share, receive and/or use your protected health information in this study?
- Staff at all the research study sites (including CCHMC)
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study.
- The members of the CCHMC Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your PHI is not misused?
People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?
You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share your PHI you need to notify the study doctor, listed on the first page of this document, in writing. Your request will be effective immediately and no new PHI about you will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?
Your permission will expire at the end of the study. If the study involves the creation or maintenance of a research database repository, this authorization will not expire.

Will your other medical care be impacted?
By signing this document you agree for you to participate in this research study and give permission to CCHMC to use and share your PHI for the purpose of this research study. If you refuse to sign this document you will not be able to participate in the study. However, your rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you should participate in this research you will document your permission by signature below.

You will receive a copy of this signed document for your records.

_____
Printed Name of Research Participant

_____ _____
Signature of Research Participant Indicating Consent or Assent — Date

_____ _____
Signature of Individual Obtaining Consent — Date