

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

STUDY TITLE: Genetics of Left Ventricular Outflow Tract Malformations

STUDY SPONSOR: National Institutes of Health

STUDY DOCTOR: Kim L McBride, MD

CONTACT TELEPHONE NUMBER: 614 722-2000 (24 hours a day, 7 days a week)

SUBJECT'S NAME: _____

DATE OF BIRTH: _____

1) INTRODUCTION

We invite you to be in this research study because you, your child, or another member of your family has a heart defect, specifically aortic stenosis, bicuspid aortic valve, coarctation of the aorta, hypoplastic left heart syndrome, Shone complex, mitral valve atresia, or interrupted aortic arch. These defects are grouped together and are called Left Ventricular Outflow Tract (LVOT) malformations. You will need to learn enough about this research study, its risks and benefits, to decide whether you should agree to participate. This process is called "informed consent". We must explain the study to you, and give you a chance to ask questions about anything you do not understand. It is up to you to choose if you want to be in this study. You may refuse to be in this study or quit this study at any time, and standard medical care will still be available here or at a doctor of your choice. It is important to understand that there may not be any benefit from being in this study, but we may learn something that could help others.

Before agreeing to be in this research study, it is important that you read and understand the study information in the consent form. By signing the consent form, you agree to be in this study. Subjects 9 through 17 years of age must also agree to be in the study by signing an Assent form. You will be given a signed copy of the consent and the assent form.

2) WHY ARE WE DOING THIS RESEARCH STUDY?

We hope to understand how changes in genes might cause heart defects. We believe that many heart defects are caused by genetic factors. We need to study genetic differences between people to find out whether they cause heart defects. Some cases may be caused by a defect in a single gene. Other cases seem to be caused by a combination of genes and the environment. It is important to understand heart defect genes to discover how to prevent these defects from happening in other children.

Several heart defects seem to be caused by blocked flow of blood from heart. The blockage can occur at one of the valves in the heart (aortic stenosis, bicuspid aortic valve, mitral stenosis, mitral valve atresia), or in the large blood vessel that supplies blood to the body (coarctation of the aorta, interrupted aortic arch). Sometimes the blockage can be very severe and cause the left side of the heart to grow poorly (hypoplastic left heart syndrome, Shone complex). Together, we call these defects Left Ventricular Outflow Tract (LVOT) malformations. They occur in about 8 out of 10,000 babies born. We know that heart defects can occur more than once in a family. The way to find genes that cause heart defects is to compare members of families.

3) WHERE WILL THE STUDY BE DONE AND HOW MANY SUBJECTS WILL TAKE PART?

This study will be done at Nationwide Children's Hospital. We hope to have about 1500 subjects here at this hospital, 500 with heart defects and 1000 relatives.

Consent obtained by
Investigator or Study Coordinator

Initials _____

4) WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

We are collecting samples from patients with several forms of heart defects that were mentioned in the introduction. We will obtain medical records to confirm all diagnoses. We will also get samples from parents and some family members. Blood specimens will be collected from up to 500 children with these heart defects and 1000 people who are parents or relatives of children affected with LVOT heart defects. The blood specimens will be used to make permanent cell lines and/or to extract DNA (the genetic material). The DNA will be tested for many genetic markers to determine if there is an association between the heart defect and one or more markers. Left over tissue removed during an operation will also be used to study the gene activities. We expect the collection to last for 5 years, but the testing may take longer.

Here are some facts to consider before you agree to participate:

1. Samples will be given a code number before they are analyzed.
2. The samples will be used only for research on congenital heart defects, unless you give us permission to use your sample for other research.
3. We will not be able to give you individual results from the study because the genetic testing is not being carried out in a clinical lab. We will not give your results to anyone else including your doctors. If we find something in your research testing that can be used to help you, we will ask your permission to give the result to a clinical lab that can then confirm the results.
4. Dr. McBride will give you information about the risk of having another child with a birth defect if you want. The results of the research may not change what your risk may be.
5. Your samples will not be available to you for any other kind of non-research or medical testing.
6. The samples may be transferred to other qualified investigators who are studying the causes of heart defects.
7. The samples will not be sold to anyone.
8. So that more people would benefit from this research, the National Institutes of Health (NIH, the sponsor of this research) has requested that we share some information about you and results of the tests we do on your sample (blood or saliva). The only information about you that we will share is your type of heart defect, your sex and race, and your test results from this research. No information that might identify who you are will be shared.
9. Procedures
 - You will be one of approximately 1500 subjects to be asked to participate in this study.
 - You will be asked to complete a questionnaire and if necessary, the investigator or his assistant will help you to answer questions about your family history and medical problems.
 - Ten (10) ml (2/3 tablespoons) of blood will be drawn from your arm if you are an adult
or
 - Five (5) ml (1 teaspoon) of blood will be drawn from your child's arm if he/she is an infant

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If you are having (or had) an operation on your heart for your heart defect, we would like to obtain any left over tissue samples removed during surgery. The tissue removed by your surgeon will be obtained from the pathology lab after all routine testing is completed. It will be studied to see which genes are active in the heart, the valves, or blood vessels. Please check YES if you agree to let us use the left over tissue, check NO if you do not want us to use this tissue.

YES _____ NO _____ Initials _____

10. Your sample may be stored indefinitely. From time to time, other researchers who are interested in medical problems other than those related to heart defects may approach us. Please check YES if you agree to let someone use any left over blood and tissue for other research questions, check NO if you do not want the samples to be used in other research.

YES _____ NO _____ Initials _____

5) **WHAT BAD THINGS CAN POSSIBLY HAPPEN DURING THIS STUDY?**

Blood draws/IV's, (putting a needle in a vein), can cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. EMLA[®] cream may be used to numb the skin to decrease the discomfort, if needed. Although there are no known side effects from EMLA[®], skin irritation or an allergic reaction is possible.

There is a risk of hearing unsettling information if the results of the genetics testing are shared with you. Changes in genes may mean your family has a higher risk of having a child with a heart defect. It is possible that non-paternity could be discovered in this study. The genetic tests used in this work could reveal that the individual who donates a sample as the patient's father is not the true biological father. This information will be kept confidential, unless you otherwise authorize its release.

Completing the questionnaire may make you uncomfortable.

6) **WHAT GOOD THINGS CAN POSSIBLY HAPPEN DURING THIS STUDY?**

Finding a minor heart defect in you, like bicuspid aortic valve, that may cause aortic or valve disease in the future that could be treated earlier to prevent problems.

However, you may receive no benefit from participating in this study.

7) **WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?**

If being in this study causes injury to your child, Nationwide Children's Hospital will provide medical care. If being in this study causes injury to your child, neither Nationwide Children's Hospital nor the study doctors will pay for care. Your insurance company may or may not pay for a study related injury. Under certain circumstances, the Sponsor (NIH) might pay for study related injury, but they are not required to do so. It is possible that you might have to pay for all the medical care required for treatment of a study-related injury to your child, but you have rights under state or federal laws to ask that costs of medical care be paid by someone else.

8) **OTHER IMPORTANT INFORMATION**

The Study Doctor is being paid by the NIH for the time and knowledge needed to do this study.

All subjects' names will be added to a database. The database shows who participated in this study and when. We may also use the database information to contact you for future research studies.

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If we find out any new information during this study that might affect a subject's health or change your mind about being in this study, a study staff member will contact you. It is your responsibility to make sure we have your current address and phone number.

Being in more than one research study at the same time may cause injury. You should tell the Study Doctor about being in any other research study. The Study Doctor will decide if it is OK to be in more than one study at the same time

Some new products might be developed and sold because of the research done on your blood or tissue but you will not receive money for this.

9) **SPECIAL INFORMATION ABOUT PREGNANCY:** N/A

10) **WHAT WILL HAPPEN IF NEW TREATMENT INFORMATION IS FOUND OUT?**

If we find out any new information during this study that might make you change your mind about being in this study or might affect your health, a study staff member will call you.

11) **WHAT OTHER TREATMENTS ARE THERE?** N/A

12) **WHAT WILL HAPPEN IF I DO NOT FINISH THIS STUDY?** N/A.

13) **WILL THERE BE ANY COSTS TO ME?**

It will not cost you anything to be in this study. To pay for your time and inconvenience, your family will receive a \$25.00 gift card.

14) **HOW WILL MY STUDY INFORMATION BE KEPT PRIVATE?**

Information collected for this study will be kept confidential. To help us protect your privacy, we have obtained a **Certificate of Confidentiality** from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

A Federal law, called the **Genetic Information Nondiscrimination Act (GINA)**, generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.

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- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009. Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Information used and/or disclosed (shared with someone outside of Nationwide Children's Hospital) may include information that can identify you. This is called "protected health information" or PHI. By agreeing to be in this study, you are giving permission or authorizing the Study Director and study staff to collect, use, and disclose your PHI for this research study. Information collected is the property of The Research Institute at Nationwide Children's Hospital. In the event of any publication regarding this study, you and/or your child's identity will not be revealed.

- **People or Companies authorized to use, disclose, and receive PHI collected or created by this research study:**
U.S. Department of Health and Human Services, NIH.
Because of the need to give information to these people, absolute confidentiality cannot be guaranteed. Information given to these people may no longer be protected by federal privacy rules.
- **PHI that may be used or disclosed:**
Name, date of birth, sex, diagnosis, results of genetic tests
- **Reason(s) why the use or disclosure is being made:**
Federal law wants us to get your permission to use your protected health information for this study. Your signature on this form means that you give us permission to use your protected health information for this research study. People who give medical care and ensure quality from the institutions where the research is being done, the sponsor(s) listed in the sections above, representatives of the sponsor, and regulatory agencies such as the U.S. Department of Health and Human Services will be allowed to look at sections of your medical and research records related to this study. Because of the need for the investigator and study staff to release information to these parties, complete privacy cannot be guaranteed.
- If you have a bad outcome or adverse event from being in this study, the Study Director and staff or other health care providers may need to look at your entire medical records.
- The PHI collected or created under this research study will be used or disclosed as needed until the end of the study. The records of this study will be kept for an indefinite period of time.
- You may decide not to authorize the use and disclosure of your PHI, however, you may not be able to be in this study. If you agree to be in this study and later decide to withdraw, you may also withdraw your authorization to use your PHI. This request must be made in writing to the Study Director. If you withdraw your authorization, no new PHI may be collected and the PHI already collected may not be used unless it has already been used or is needed to complete the study analysis and reports.

Dr. Kim McBride keeps a database of all subjects who participate in a research study. This database is used to keep track of the research studies Dr. Kim McBride conducts and who participated in each study. This database is also used to contact people about future studies. Only Dr. Kim McBride and his staff have access to this database.

15) WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have questions about anything while on this study, you have 24 hour access to talk to your Study Doctor at 614-722-2000.

If you have questions or are worried about your rights as a research volunteer, please call (614) 722-2874, Nationwide Children's Hospital, Institutional Review Board, (IRB, a committee that reviews all human subjects' research).

Consent obtained by
Investigator or Study Coordinator

Initials _____

Subject's Name _____

Date of Birth _____

SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE STATEMENT

I have read this consent form and have had a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the Study Doctor. By signing this consent form, I certify that all health information I have given is true and correct to the best of my knowledge.

I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. I understand that my right to my patient information that is created or collected by Nationwide Children's Hospital in the course of this research can be temporarily suspended for as long as the research is in progress. I also understand that my right to access will be reinstated upon completion of this research.

I agree to participate in this study. I will be given a copy of this consent form with all the signatures for my own records.

CONSENT SIGNATURES

SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE

DATE SIGNED

SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE

DATE SIGNED

PERSON OBTAINING CONSENT

I certify that I have explained the research, its purposes, and the procedures to the subject or subject's legal representative before requesting their signature.

DATE SIGNED

STUDY INVESTIGATOR

DATE SIGNED