Complement and Cardiovascular Risk in Adolescents
NCT02821104
11/5/2020

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

STUDY TITLE: Complement and cardiovascular risk in adolescents

PRINCIPAL INVESTIGATOR: Robert P. Hoffman, MD

CONTACT TELEPHONE NUMBER: 614-722-4425

STUDY SPONSOR: American Heart Association

SUBJECT'S NAME: _____ DATE OF BIRTH: _____

NOTE: The words "you" and "your" are used in this consent form. These words refer to the study volunteer whether a child or an adult.

1) INTRODUCTION

We invite you to be in this research study because you are a healthy individual between 12 and 18 years of age without significant medical illness. You cannot have taken any medications except oral contraceptives in females for two weeks prior to being in the study.

Participation is voluntary. Using this form as a guide, we will explain the study to you. If you have any questions about the study, please ask. Once you understand this study, we will ask you to decide whether you would like to participate or not. By signing this form, you agree to be in this study. If you do not want to be involved with this study, all regular and standard medical care will still be available to you here or at another institution. You also have the right to leave this study at any time, even if you agree to join now.

Because this study involves a child between 12 and 18 years of age, the child will receive an explanation of the study in a separate form, called an Assent form. If they agree to be in the study, they will be asked to sign this form.

You will be given a signed and dated copy of the consent and the assent form.

2) WHY ARE WE DOING THIS RESEARCH STUDY?

This is a study to find out how a part of the immune system called complement affects risk of future diabetes, high blood pressure, heart disease or stroke. Evidence suggests that these diseases which are major causes of death in adults begin in adolescents. There are specific tests that may identify adolescents at risk for these diseases. Complement is part of the immune system. The immune system helps your body fight diseases. Complement increases inflammation. Long-term increases in inflammation increase your risk of cardiovascular disease and diabetes. There is evidence that some people have genetic differences in two complement genes called C3 and C4 that are associated with increased risk in adults. The investigators are testing whether this is true in adolescents. This

information will help doctors identify adolescents at risk for future cardiovascular risk and also help us identify ways to reduce the risk.

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

This study will be done at in the Clinical Research Center (CRC) at the Wexner Medical Center at The Ohio State University. We hope to enroll 100 participants.

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

Only one study visit is necessary. You will come to the CRC at 8 AM. The visit will last approximately 4 hours. You should not eat after 10 PM the night before.

After you agree to participate a medical history will be taken and then a brief physical examination performed. This physical examination will include assessment of pubertal status by examining your breasts or genitalia. For girls a pregnancy test will be done. Your height and weight will be measured. We will also measure you're the distance around your waist.

You will then be asked to put on swimsuit. This is necessary for measurement of how much body fat you have. This is done with device called a BodPod. This looks like a large egg and you will sit inside of it. The investigators can tell how much fat you have by how much you weigh and how much space you take up.

After the BodPod you can put your regular clothes back on if you wish. We will then do a measurement of how your stiff your arteries are. A small pencil like device will be held on the artery in the left wrist. The device is not sharp and will not hurt. The investigator will move the device around until a good reading is obtained. You will need to hold your wrist still. This may take 5 minutes.

Next we will measure how the lining of your blood vessels, called the endothelium, functions. Two blood pressure cuffs will be put on your arm. One will be put at the wrist; the other will be on the upper arm. An elastic wire will be put around your lower arm, also. This equipment is used to measure the blood flow to your arm. When the blood flow is being measured the cuff on the wrist will be inflated to a high pressure to stop blood flow to your hand and the cuff on the upper arm will be inflated at low pressure off and on every 15 seconds. This will be done for 2 minutes. To measure endothelial function, the upper arm cuff will then be inflated to a high pressure to cut off blood flow to the arm for 5 minutes. The upper arm cuff will then be released and the cuffs will go up and down as before for 1 minute. This entire test will take 8 minutes and the upper arm cuff will stop flow to your arm for 5 minutes of these 8 minutes. The lower cuff will cut off blood supply to your hand for 8 minutes. We will use a standard blood pressure machine to measure blood pressure in your other arm.

After the test is done an intravenous catheter will be place in a vein in one arm. The catheter will be used to draw several blood samples. The first sample will be about 5 teaspoons. This will be used to measure markers of inflammation and blood vessels function. Specific tests that will be measured are plasma glucose, insulin, lipids, CRP, IL6, fibrinogen, PAI1, endothelin 1 levels. Part of the sample will also be used to measure levels of complement in the blood and to assess the complement genes.

After the first blood sample is taken we will do an oral glucose tolerance test. For this test you will be given a sugary drink we will ask you to drink it over 5 minutes. Small blood samples (1/2) teaspoon will be taken from the intravenous catheter 30, 60, 90, and 120 minutes after the drink. These will be used to measure how much glucose and insulin are in your blood. The test is used to measure how will your body makes and responds to insulin.

After the glucose tolerance test you will be given a meal and can leave.

We will be testing your (blood or tissue or DNA) to measure two specific changes in the C3 gene and how many C4 genes. Differences in these genes are not linked to any specific medical condition. Having a specific gene does not mean you will definitely get or not get any disease. We will also preserve some of the white blood cells called lymphoblasts in the laboratory so that in the future we will be able to test other genes that may be of interest. After the initial study is complete we will eliminate identifying information so that no one will be able to link any findings to you. You will not be told the results of the gene testing. No information gained from the gene testing would change your regular medical care.

The blood and oral glucose tolerance tests may provide information that we were not specifically looking for in this study. This information is called "incidental findings". We may find that you have diabetes or have high levels of cholesterol that might require treatment. We will discuss these results with you if we believe that they may have a significant impact on your health or family's health. If you ask us to do so, we can also help you set up follow-up meetings with the personal physician that you identify to us or other medical professionals who are not involved in this study but who can discuss this information with you. These follow-up visits will not be part of this study. Therefore, you and your insurance company would be responsible for any fees and costs related to them.

You will not receive any money or other compensation for any new products that might be developed or sold from research that used your blood or tissue.

5) WHAT ARE THE RISKS OF BEING IN THIS STUDY?

It is important that you give the study staff a complete medical history. Not giving them this information or not completely following the directions of the study could harm you.

You may feel like you are being closed in on when you sit in the BodPod. It will only take a couple of minutes. If you feel too anxious let us know and we will stop.

The stopping of the blood supply to the hand for 8 minutes may make your hand feel numb or tingle. The feeling will go away when the pressure is released. If this becomes too uncomfortable you can ask the investigators to stop.

Starting the intravenous catheter and drawing blood may cause pain bleeding, infection, bruising, or inflammation at the site of the blood site; fainting is also a possible adverse effect.

You may not like the taste of the sugary drink and this could make you nauseous or vomit.

6) SPECIAL INFORMATION ABOUT PREGNANCY:

If you are pregnant or become pregnant while taking part in this research, the study medicine or study procedures may cause unknown harm to both your pregnancy or your fetus. Participation in this study will not be offered to females who are pregnant or breast-feeding. A pregnancy test will be done for any female who is sexually mature enough (started having periods), to become pregnant. The pregnancy test may be done using blood and/or urine. You (and your parents) will be told the results of the pregnancy test.

7) ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

Although there will be no benefit to you from being in this study, we hope to learn something that could help others.

8) WHAT ARE THE COSTS AND REIMBURSEMENTS?

All costs related to the research parts of this study will be covered by the research team. However, the parts of the study that would be done for routine clinical care will be billed to you and to your insurance company or third party payer. You may have to pay any costs that the insurance company or third party payer does not pay. The study team will discuss these costs with you.

There will be additional costs related to travel and meals during this study. We will not provide money to help with these costs. A parking voucher will be provided each time you come in for a study visit. This reimbursement may be taxable. The study team will discuss this with you.

For your time and inconvenience, you (study participant) will receive $100 for the study visit.

If you receive more than $600 in a calendar year from participating in this and/or other studies, you will be asked for your social security number and you will be issued a 1099 tax form to file with your income taxes.

9) WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the procedures that are part of the Study, you should seek medical treatment for the injuries and tell the Principal Investigator as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

In most cases, this care will be billed to your health insurance company or whoever usually pays for your health care at the usual charges, but some insurance companies will not pay for care related to a study. If the care is provided at Nationwide Children's Hospital, we make no commitment to pay for the medical care provided to you. No funds have been set aside to compensate you in the event of injury. If no one else pays for your care, you may have to pay for the cost of this care. This does not mean that you give up any of your legal rights to seek compensation for your injuries.

10) WHAT HAPPENS IF I DO NOT FINISH THIS STUDY?

It is your choice to be in this study. You may decide to stop being in this study at any time. If you decide to stop being in this study you must tell the Principal Investigator or the study coordinator to see if there are any medical issues about stopping. If you stop being in the study, there will not be a penalty or loss of benefits to which you are otherwise entitled.

If at any time the Principal Investigator believes that this study is not good for you, the study staff will contact you about stopping. If the study instructions are not followed, participation in the study may also be stopped.

11) OTHER IMPORTANT INFORMATION

Being in more than one research study at the same time may cause injury. Please tell us if you are in any other research study so a decision can be made about being in more than one study at the same time. We may need to notify the other study team to see if you can participate in this study.

If you are an employee of Nationwide Children's Hospital or the Research Institute at Nationwide Children's Hospital, your job or performance appraisal will not be affected in any way if you decline to participate or withdraw your consent to participate in this study.

The final study results will not be shared with you individually.

Nationwide Children's Hospital is a teaching hospital and we are committed to doing research. Doing research will enable us to learn and provide the best care for our patients and families. You may be asked to participate in other research studies in the future. You have the right to decide to participate or decline to participate in any future studies. We will not share your contact information with researchers outside Nationwide Children's Hospital.

12) HOW WILL MY STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study includes information that can identify you. This is called "protected health information" or PHI. By agreeing to be in this study, you are giving permission to Robert Hoffman and the study staff to collect, use, and disclose your PHI for this research study and for future research purposes (including purposes that are currently unknown) unless otherwise allowed by applicable laws. Information collected is the property of Nationwide Children's Hospital, one of its affiliated entities, or the Sponsor.

PHI that may be used or disclosed: Your name, address, telephone number, birthdate and admission date.

People or Companies authorized to use, disclose, and receive PHI collected or created by this research study:

- PI and study staff
- The Nationwide Children's Hospital Institutional Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- Sponsor: American Heart Association

- The Office for Human Research Protections (OHRP) (the federal government office that oversees human subject research)

Because of the need to give information to these people, absolute confidentiality cannot be guaranteed. Information given to these people may be further disclosed by them and no longer be protected by federal privacy rules.

Reason(s) why the use or disclosure is being made: To contact you in the future for possible participation in follow-up studies.

You may decide not to authorize the use and disclosure of your PHI. However, if it is needed for this study, you will not be able to be in this study. If you agree to be in this study and later decide to withdraw your participation, you may withdraw your authorization to use your PHI. This request must be made in writing to the Principal Investigator at

Nationwide Children's Hospital
Department of Endocrinology
700 Children's Drive
Columbus, OH 43205

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.

There is a risk that someone could get access to the information (data) we have collected about you. If those data suggested something serious about your health, it could be misused. For example, it could be used to make it harder for you to get or keep a job or insurance. The Genetic Information Nondiscrimination Act of 2008 (GINA) says that group and individual health insurers may not use your genetic information to determine whether you are eligible for insurance, how much you have to pay, nor can they request or require that you take a genetic test. We cannot guarantee that this will fully protect you. Your privacy and the confidentiality of your data are very important to us. We will make every effort to protect them.

PHI will only be shared with the groups listed above, but if you have a bad outcome or adverse event from being in this study, the Principal Investigator and staff or other health care providers may need to look at your entire medical records. In the event of any publication regarding this or any future studies, your identity will not be revealed.

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 and your authorization to use or disclose your PHI will not expire.

As stated above, your PHI may be used or disclosed for future research purposes, and as part of such future research purposes, your PHI may even be disclosed to people or entities that are not listed above, such as other researchers not involved with this study, government agencies, research foundations, or pharmaceutical or device companies sponsoring future research. This future research may be related to your medical problem, but it may be related to other diseases or conditions as well. Any future research projects, however, will be reviewed and approved by an Institutional Review Board, which protects the rights, welfare, and safety of human research subjects.

I agree to allow my PHI to be stored and used for future research as described above: (initial your choice)

_____ YES _____ NO

The Principal Investigator may want to do additional studies regarding how the complement genes affect changes in risk over time. I agree to be contacted regarding these future studies.

_____ YES _____ NO

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

If you have questions about anything while on this study or you have been injured by the research, you may contact the Principal Investigator at 614-722-4425 , Monday – Friday, between 8:00AM and 4:30 PM.

If you have questions, concerns, or complaints about the research; if you have questions about your rights as a research volunteer; if you cannot reach the Principal Investigator; or if you want to call someone else - please call (614) 722-2708, Nationwide Children's Hospital Institutional Review Board, (IRB, the committee that reviews all research involving human subjects at Nationwide Children's Hospital).

Subject's Name _____Date of Birth_____

SUBJECT or SUBJECT'S PARENT OR PERSON AUTHORIZED TO CONSENT ON BEHALF OF THE CHILD (SUBJECT TO THE SUBJECT'S GENERAL MEDICAL CARE)

I have read this consent form and I have had an opportunity to ask questions about this research study. These questions have been answered to my satisfaction. If I have more questions about participating in this study or a research-related injury, I may contact the Principal Investigator. 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. If allowed by law, I understand that my right to any information that is created or collected by Nationwide Children's Hospital for this study can be temporarily suspended if necessary for the purposes of this research project. I also understand that my right to access to this information from this study will be reinstated upon completion of this research unless I have been told by the Principal Investigator that I will not receive study results.

I agree to participate in this study or I give permission for my child 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 & TIME AM/PM**

_____ _____
SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE **DATE & TIME AM/PM**

Permission of the second parent not obtained because (select all that apply):
_____ Not required by the IRB (risk level 1 or 2).
_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

_____ _____
PERSON OBTAINING CONSENT **DATE & TIME AM/PM**
I certify that I have explained the research, its purposes, and the procedures to the subject or the subject's legal representatives before requesting their signatures.

.