

PATIENT INFORMATION AND CONSENT FORM

STUDY TITLE: Cytokine Dysregulation, Viruses, and Childhood Asthma

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CO-INVESTIGATOR: James E. Gern, M.D.

INTRODUCTION:

This informed consent describes the procedures and your role as a participant in this research study. Before agreeing to participate in this research study, it is important that you read and understand the following explanations of the proposed procedures. Please read this information carefully and do not hesitate to ask the study doctor or study coordinator any questions. You must sign this informed consent before you and your child may enter the study.

THE NATURE AND PURPOSE OF THIS STUDY:

Asthma is a growing medical concern particularly in children, causing recurrent episodes of wheezing, breathlessness, chest tightness, and cough particularly at night and/or in the early morning. Although asthma may begin soon after birth, the natural history of the disease is poorly understood. Both genetic (one or both parents having a history of allergies or asthma) and environmental (specifically viral respiratory tract infections) factors have been considered to be important in the development of asthma. Identification of genetic markers of asthma may allow screening of high-risk children, permitting better targeting of avoidance measures. Many young children wheeze during viral respiratory infections, but the relationship of these episodes to the development of asthma later in life are not well understood. Studies of young children are needed to test the suspicion that genetic or inheritable factors, combined with early lower respiratory infections, may predict the future development of asthma. *The main purpose of this study is to evaluate whether the development of childhood asthma requires the presence of a genetic component and an environmental component (development of a clinically significant lower respiratory tract infection in the first year of life).* If you agree to participate in this study, you will be one of approximately 200 families enrolled. This study is being conducted at this center only and is funded by the National Institutes of Health (NIH).

WHAT DOES STUDY PARTICIPATION INVOLVE?

This study will be conducted over a three year period (approximately). It will begin at the time you sign this consent and will continue until your child is three years old. You may be eligible for this study if you are expectant parents, at least one of which has a history of allergies or asthma. Eligibility will be determined at a prescreen visit before the birth of your baby. If you are eligible and do decide to participate, you will need to visit the study center at least six times during the three years of the study. Three of the study visits will take place at your child's primary care provider's office. Each of these visits will last approximately ½ to 1 hour.

Study Procedures

Parent medical and family history (once)

Update parent allergy/asthma/family history (nine times)

Child physical exam (nine times)

Parent allergy skin testing (one time for each parent)

Parent blood draw for laboratory tests (one time for each parent)

Cord blood sample at birth

Child blood draw for laboratory tests (three times)

Child questionnaire (nine times)

Nasal mucus sampling from child (minimum nine times and with any occurrence of lower respiratory infection)

Nasopharyngeal throat swab samples from child (minimum nine times and with any occurrence of lower respiratory infection symptoms)

Explanation of study procedures

Blood draws To evaluate the possible genetic phenotype (hereditary) and environmental components of asthma, blood samples will need to be obtained from both parents and your child. The blood samples will be obtained from a vein and will be tested for immunologic factors to help us learn more about how heredity influences the development of allergies and asthma. Your child's blood will also be evaluated to see how the type of viral infections he/she may have had has affected these factors. Your baby's blood (approximately 1 tablespoon) will be obtained three times during the three years of the study. One blood sample will be obtained from each parent.

DNA Testing As an additional question, we are asking you to consider permitting us to processes and to store a portion of the blood sample obtained from you and your child for future DNA examination. We anticipate that new knowledge about the asthma and allergy genes may be available in the next several years. Therefore, we are asking you now to consider the storage of blood samples in anticipation of these future scientific discoveries. The blood samples from you and your child could contribute to a better understanding as to how and why asthma and allergies may be inherited.

If you agree to the storage of blood for future DNA research, it is essential that we are able to update your medical history at the time the DNA would be evaluated in the future. Therefore, please let the study coordinator know if you move or change doctors so that you can provide us with this information. If significant changes in your health do occur in the future, we may ask your permission to obtain a second blood sample to permit a comparison with the sample to be drawn shortly. Dr. Lemanske may also want

to use your stored DNA as a shared research effort with other researchers investigating the origins of childhood asthma.

Since this is a research project and not part of your regular medical care, we do not intend to use the results of this study to determine your risk of developing asthma or allergic disease. While we hope this research may help someday lead to a test that will identify people with an increased risk of asthma or allergic disease, we do not know if that will happen. Even if a test is developed, a number of problems may occur that can make it risky to use the test to diagnose patients. The test may not be accurate or reliable for everyone, it may not lead to more effective medical treatment, or it might actually be harmful (see the “Risks” section). For these reasons, no results from the testing of your blood sample will be shared with you, your doctor, or anyone else. In other words, this part of the study will not help you understand your family’s risk of developing asthma or allergies. See the “Alternatives” section for other ways your risk may be determined.

It is important for you to know that if you choose not to have some of your or your child’s blood stored for future DNA analysis, you and your child are still eligible to participate fully in this research project.

Let us know whether Dr. Lemanske or others may use you and your child’s DNA for future research by putting your initials by as many choices that apply:

MOTHER:

we may not use you or your child’s DNA for any future research or share it with other investigators

we may use you and your child’s DNA for research only as it relates to asthma or allergic disease at our site.

we may use you and your child’s DNA for asthma or allergy research being conducted at other sites. All identifying information will be removed from the specimen prior to sharing with another researcher.

we may use you and your child’s DNA for other asthma and allergy research or share it with other researchers only after contacting you and getting your permission

FATHER:

we may not use you or your child’s DNA for any future research or share it with other investigators

we may use you and your child’s DNA for research only as it relates to asthma or allergic disease at our site.

we may use you and your child’s DNA for asthma or allergy research being conducted at other sites. All identifying information will be removed from the specimen prior to sharing with another researcher.

we may use you and your child’s DNA for other asthma and allergy research or share it with other researchers only after contacting you and getting your permission

Allergy skin testing Expectant fathers will be skin tested at the pre-screen visit and mothers within the first two months following the birth of your baby. Fourteen drops of dissolved extract of common allergens (such as house dust mite, pollen, grass) will be placed on the skin of your forearm and your underlying skin will be lightly pricked with a sterile disposable needle. Fifteen minutes later, your skin will be inspected for localized redness and swelling.

Nasal mucus sampling A bulb or regular syringe/tube will be used to collect the mucus from your child's nose. Up to three milliliters (about half a teaspoon-dependant upon size of child) of sterile salt water will be administered to each nostril by squeezing the bulb/regular syringe. The bulb/regular syringe will then be released, suctioning the fluid back into the bulb/syringe to help wash out the small amount of nasal secretions that are normally present in all noses.

Throat swabs To collect the sample, your child's throat will be swabbed with a cotton-tipped applicator using the normal procedure for throat cultures.

Visits:

Prescreen Visit:

This visit will take approximately ½ to 1 hour and must occur before the birth of your baby. It is preferable that both parents be present at this study visit; however, it is not required. During this visit at the study center, the study coordinator will ask you questions about your medical history, particularly your history of allergies and asthma. The study coordinator will also perform allergy skin testing on expectant fathers to help determine whether you are eligible to participate. Mothers will have allergy skin testing and a blood sample obtained after the birth of your child. This visit will be scheduled at the study center within two months after the birth of your child at your convenience. Fathers will have a blood sample drawn after the birth of the baby as well. The blood samples will be tested for immunologic factors to help us learn more about how heredity influences the development of allergies and asthma.

Birth of your baby:

There is a possibility that you may not be eligible for the study even after you have signed the consent form. This may be the case if your infant would have an Apgar score of six or less at five minutes of age. An Apgar score is given at birth and again five minutes after birth by a physician as an indicator of a newborn's health status. If your infant is delivered prematurely (before 37 weeks gestation) or very late in gestation (43 weeks or more) you will not be eligible. Similarly, if your baby is born with any significant birth defects or newborn illnesses, you will not be able to participate. If your family is eligible after the birth of your baby, a sample of your baby's cord blood will be obtained at the hospital. This blood will only be tested for immunologic factors to help us learn more about how heredity influences the development of allergies and asthma. This blood is obtained from the placenta or "afterbirth" tissue and does not involve any discomfort to your newborn baby.

Visits 1 and 2:

These visits will take approximately 1 hour (this includes the exam with your child's MD,

the study portion of the visit will add approximately 15-30 minutes) and will be done when your baby is approximately 2 and 4 months old during scheduled well-baby checks at your child's primary health care provider's office. A brief update of the parental questionnaire completed at the prescreen visit will be done. A child's questionnaire will be completed to evaluate your child's health since birth. Questions about your home environment such as where your child usually sleeps will also be asked to help us evaluate the role of environmental factors on the possible development of allergies or asthma. Your child will be seen by his/her primary care provider and will have a physical examination. To evaluate how viral respiratory infections may impact the development of asthma, nasal mucus/throat swab sampling will be obtained to look for viruses in the samples.

Visit 3:

This visit will be performed when your child is approximately 6 months old. The visit will take approximately 1 hour and will be scheduled at the study center. The procedures at this visit include a physical examination of your child by a physician, parent and child health questionnaires, and nasal mucus/throat swab samples.

Visit 4:

This visit will be performed when your child is approximately 9 months old. The visit will take approximately 1 hour and will be scheduled at either the study center or your child's primary health care provider's office. The procedures at this visit include a physical examination of your child by a physician, parent and child health questionnaires, and nasal mucus/throat swab samples.

Visit 5:

This visit will be completed when your child is approximately one year old and will be scheduled at the study center. Procedures at this visit include a physical examination of your child by a physician, parent and child health questionnaires, nasal mucus /throat swab samples, and blood samples from the child.

Visit 6:

This visit will be done when your child is approximately 1½ years old. Visit procedures will be the same as at visit 3.

Visit 7:

This visit will be done when your child is two years old and will be identical to visit 5.

Visit 8:

This visit will be performed when your child is 2½ years old and will be the same as procedures outlined for visit 3.

Visit 9:

This visit will be done when your child is three years old and is the same as visit 5.

To evaluate how viral respiratory infections may impact the development of asthma, collection of nasal mucus and throat swab samples will also be required when your child

becomes ill with certain respiratory infection symptoms. Respiratory infections are characterized by fever, wheezing, and/or coughing, and chest/nasal congestion. The collection of these samples will be done at the time of presentation to your child's physicians clinic for a "sick visit", as a home visit, or at the study center and should ideally be performed within 72 hours of the onset of his/her symptoms meeting the predetermined criteria for the study.

WHAT ARE THE BENEFITS OF STUDY PARTICIPATION?

There is not likely any direct medical benefit to you or your child for participation in this study. It may be a benefit to you and your child's primary physician to have information regarding virus identification from nasal mucus and throat samples available after sampling. The societal benefits of this study may be invaluable. The information we collect about how hereditary and environmental factors impact on the development of asthma could be helpful in addressing the issues surrounding primary prevention of childhood asthma in the future. Some people also find satisfaction in contributing to scientific knowledge.

WHAT ARE THE RISKS?

Drawing blood from a vein may cause discomfort, possible bruising or swelling at the site of injection, and on rare occasions, a minor infection may result from this procedure. You and your child may have a cream called EMLA[®] applied to your skin before the needle stick, which can decrease the hurt and may cause a rash. Side effects are unlikely with the use of EMLA[®] cream due to the small dose absorbed.

DNA will be extracted from your blood and analyzed for possible variations in certain genes related to asthma, allergic disease, and respiratory infections. Should your child develop asthma, and should this research result in the identification of a genetic link to the development of asthma, the effect of this genetic knowledge will be irrelevant for your child since the condition has already been diagnosed. Should your child not develop asthma, but through testing it is learned that your child has the genetic makeup that is associated with an increased risk for the development of asthma, there is the remote possibility that this knowledge could affect insurability for your child. However, a number of facts are important for you to know. First, no study records or testing information will be released to insurance carriers unless you so request. Second, your insurance carrier will only know that this information has been collected if you disclose it to them. Finally, it is illegal in the state of Wisconsin for employers to discriminate against you on the basis of this genetic information. Federal law provides limited protection against discrimination by insurance companies based on genetic information, but the law does not apply to every situation.

Your child may experience mild irritation at the opening of the nose where the bulb syringe is placed during the nasal mucus collection, however this is very rare. Instilling sterile buffered saline should not burn, but may feel uncomfortable for a few minutes secondary to a dripping feeling until the solution is suctioned back into the bulb syringe. There could be an extremely rare occurrence of an abrasion to the nasal lining if the child were to suddenly jerk his/her head during attempts to obtain the mucus sample. This is very unlikely since the tip of the bulb syringe is very soft and will not be

advanced into the nose to any significant extent.

Allergy skin testing carries the risk of itching and burning at the site of the test, and the discomfort of the needle prick. In extremely rare cases, exposure of allergic people to an allergen can result in "anaphylaxis", a term which describes a serious combination of medical problems including severe asthma (chest tightness, coughing, shortness of breath), hives or a rash on your skin, swelling of your skin or tongue, itchiness of your skin and fall in blood pressure. In very rare instances anaphylactic reactions can result in death. Facilities and medications are available for treatment of severe allergic reactions and anaphylaxis if they should occur and a physician will be nearby when the skin test is performed.

WHAT ALTERNATE THERAPIES TO STUDY PARTICIPATION ARE AVAILABLE?

You do not have to participate in this research. As alternatives to participating in this study, you and your child can choose not to participate or to participate in other investigational studies. You and your child would then receive the usual well baby care and check-ups. It is important to remember that this study will not help you learn your risk of asthma or allergic diseases. If you would be interested in determining your risk of developing asthma or allergic disease once such a test becomes available, reliable, and helpful, you should periodically ask your doctor or a genetic counselor if the test is available, and ask him or her to discuss its advantages and disadvantages with you. (A genetic counselor is professionally trained to help you understand what genetic test results mean and don't mean for you and members of your family).

WILL THERE BE COMPENSATION FOR INJURY?

In the event that physical injury occurs as a result of this research, medical care, including hospitalization, is available; however the University of Wisconsin, Meriter Hospital, and St. Mary's Hospital do not automatically provide reimbursement for medical care or other compensation. If physical injury is suffered in the course of the study or for more information, please notify the investigator in charge, Dr. Robert Lemanske at (608) 263-8539.

WILL THERE BE ANY COSTS TO YOU?

There will be no cost for any study-related visits, procedures, or blood tests at the study center as well as study-related nasal mucus and throat swab samples performed at your child's physicians clinic when your child is ill with certain respiratory infection symptoms.

VOLUNTARY PARTICIPATION/WITHDRAWAL FROM STUDY:

Participation in this study is entirely voluntary. You may decide not to participate or to discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled. You are encouraged to contact the study doctor or coordinator should you decide not to continue your participation in this study. Deciding not to participate will not affect your baby's medical care in any way. Although it is not anticipated, your participation in this study may be terminated by the study center if you do not follow study instructions or for administrative reasons. If you allow the storage of blood for DNA testing and once the researchers begin studying your DNA, there are

two ways you can withdraw from this aspect of the study. One is to ask Dr. Lemanske and his colleagues to remove all identifying information associated with your sample. The other is to ask them to destroy any of your remaining DNA or tissue. Both of these options (especially the second one) could be damaging to the research project, especially if the information from your sample turns out to be important. Therefore we are asking you to think very carefully about the reasons why you might change your mind, and be as sure as you can that you will not withdraw after your sample is taken. If you initially agree to the storage of blood for DNA testing, and then later decide to not allow the DNA testing to proceed,, you may still participate in all other aspects of the study if you wish.

WILL THERE BE ANY COMPENSATION?

Recognizing that this study will require extra time and effort, you will be paid \$500.00 for your participation. This amount will be prorated according to the following scale based on study visits completed:

Screening visits:	
Father Skin test & blood draw	\$25.00
Mother Skin test & blood draw (After birth of baby)	\$25.00
Visits 1-9:	\$50.00 each
	Total = \$500.00

In addition, your child will be paid a total of \$15.00 for nasal mucus and throat swab samples that are obtained from your child at the time of illness.

We highly encourage that a portion of this money be used for the betterment of your child’s development (i.e. investments, savings, or an educational fund). Usable items that will serve doubly as reminders (such as stickers, medicine droppers, magnet, etc.) will be given after every study visit in appreciation of your commitment to helping us learn more about asthma and allergic disease.

WHO WILL SEE THE STUDY RECORDS?

Your study physician and coordinator will treat your identity with professional standards of confidentiality. Your medical records may be accessed and reviewed by study personnel for the purpose of verifying medical history pertinent to determining your eligibility for study participation. Some aspects of the medical information gathered from this study (for example, the virus identification reports that will be sent to your primary care provider) may become part of your child’s permanent medical record. No DNA information collected by the study doctor and staff will become part of your permanent medical record.

Your records regarding this study may be subject to review by appropriate officials of the University of Wisconsin should the need arise. No study records or information will be released to insurance carriers unless you so request. Your insurance carrier will only know that this information has been collected if you disclose it to them. Additionally the

medical information and records gathered from this study may be submitted to the National Institutes of Health and their agents. The results of this study may be published in scientific journals or be presented at medical meetings, however you and your child will not be identified by name.

WHO WILL ANSWER QUESTIONS?

Please feel free to ask questions at any time. You may take as long as necessary to decide whether you wish to participate in this study. In addition, if you have questions concerning your rights as a research subject, you may contact one of the patient representatives at (608) 263-8009.

The doctor in charge of the study is Dr. Robert F. Lemanske, Jr. He is a pediatrician specializing in allergy and immunology and is a Professor at the University of Wisconsin Medical School. If you have any questions about this research or believe you have sustained an injury, you can reach Dr. Lemanske at his office at the University of Wisconsin at (608) 263-6180 or (608) 263-8539.

CONSENT FOR PARTICIPATION AND FUTURE USE OF DNA SAMPLES

I have read this consent form. I have voluntarily given permission for myself and my child's participation in this research project. I am aware I will receive a copy of this informed consent.

Signature (mother)

Date

Signature (father)

Date

Signature of person obtaining consent

Date

Baby's full name

(To be filled in after birth)

Signature of person recording baby's name after birth

If you have any questions or problems please contact:
Robert F. Lemanske, Jr., M.D. (608)263-8539.