

UNIVERSITY OF MICHIGAN CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. *Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.*

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title:

Placental Vascular Determinants of Fetal Growth: the GROW (Gestational Regulators of Weight) Study

1.2 Company or agency sponsoring the study:

This study is sponsored in part by the National Institutes of Health and the Doris Duke Charitable Foundation.

1.3 Names, degrees, and affiliations of the researchers conducting the study:

Vinod K. Misra, M.D., Ph.D.
Department of Pediatrics and Communicable Diseases
University of Michigan

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

This research project will help us find out more about why some babies are born smaller than others. This information is important because some babies who are born too small can have serious medical problems. We think that poor blood flow to the baby during pregnancy is an important cause of growth problems. We will look at a gene for a factor called VEGF and levels of blood factors related to VEGF. We will use ultrasound to see how these factors affect blood flow to your baby and your baby's growth. Finding relationships between VEGF, blood flow, and growth will help us better care for pregnant women to prevent poor birth outcomes.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. *A request to participate in this study does not indicate that there is any prior concern about you or your baby's health. We are contacting all women seeking prenatal care at the U of M who are early in their pregnancies and who may be eligible to participate in this study.* You do not have to participate if you do not wish. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

You have been invited to take part in this study because you are receiving prenatal care through the University of Michigan Health System and you are fewer than 10 weeks pregnant with one baby.

Eligible participants:

- are between the ages of 18-45;
- are carrying a single, intrauterine pregnancy of less than 10 weeks gestation;
- did not conceive this pregnancy using donor eggs, in-vitro fertilization, intracytoplasmic sperm injection, or gamete intrafallopian transfer;
- did not undergo therapeutic pregnancy reduction for this pregnancy.

3.2 How many people (subjects) are expected to take part in this study?

We expect to enroll about 450 pregnant women through the University of Michigan Health System into this study.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

If you agree to join this study, you will be asked to attend 5 study visits.

You will be asked to come for an initial study visit at the University of Michigan Hospital when you are 6-10 weeks pregnant; this is earlier than you would usually begin receiving prenatal care. You will then be asked to return for 4 more study visits at 10-14 weeks, 16-20 weeks, 22-26 weeks and 32-36 weeks of pregnancy.

Each study visit will consist of an interview, an ultrasound of your baby, and a blood draw. You will also have your height, weight, and blood pressure checked. We will review your medical records to obtain your health information and information about your baby at delivery.

Interviews: The interview will collect information about your prior medical history, health behaviors, and your current pregnancy. Specifically, we will ask you about your education, income, medical conditions, medications, and tobacco and alcohol exposure. We will also ask a few questions about your baby's biological father. At each visit, you will be asked if these factors have changed since your last visit. Each interview will be performed by a trained staff member affiliated with our study and should take no longer than 15-30 minutes.

Blood Samples: At the first visit, we will draw seven 10 cc samples (about five tablespoons) of blood.

Two samples will be used to determine which one of two types of a gene called VEGF that you carry. This is one of many genes that provide a set of instructions that affect your physical characteristics (like height, weight, and blood pressure) and may influence the health of you or your baby. Four samples will be used to measure the levels of several factors related to VEGF that may affect how blood vessels form in the placenta. Other tubes will be used to measure your nutritional status and other factors which may affect fetal growth.

At each follow-up visit, we will draw five 10 cc samples (about four tablespoons) of blood to measure the levels of several blood factors related to VEGF and your nutritional status.

When you deliver your baby, we will also collect a sample of your baby's cord blood from the placenta, using a sample already drawn by the hospital staff. This sample will be used to determine which one of two types of the VEGF gene your baby carries. Your baby will not need to have any extra blood drawn for this research study.

Buccal Swabs: At delivery, a buccal sample will be obtained from your baby by gently brushing the inside of the cheek with 3 to 5 soft, sterile brushes or swabs. We will extract a small amount of DNA from these brushes to determine which one of two types of the VEGF gene your baby carries.

Urine Samples: At your first visit and fourth follow up study visits, we will ask for a urine sample. We will use this sample only to determine your exposure to cigarette smoke and nicotine.

Microbiomics samples: At each study visit, we will ask you to provide three samples that will be analyzed for the presence of bacteria and other microbes that commonly live on the body. These samples include: a saliva sample obtained by chewing a small piece of sterile cotton; a vaginal fluid sample obtained by swabbing the inside of your vagina with a sterile cotton swab; and an anal swab obtained by wiping the outside of your anus with a sterile cotton swab.

Ultrasounds: At each visit, an ultrasound of the baby will be performed. A transducer sends out sound waves that are changed into a picture, which is seen on a television screen. There will be minimal discomfort to you. At the first visit, we will confirm your pregnancy, determine if there is more than one baby, determine the baby's location, and measure the length of the baby to determine its age. At follow-up visits, we will measure the baby's head size, abdominal size, abdominal fat, and thigh bone length. At each of the visits, we will use ultrasound to estimate your body composition and to measure the blood flow to the baby.

Placental Samples: After your baby is born we will retrieve your placenta after the hospital has done all necessary studies. The placenta will be examined under a microscope to study how well it grew and how well the blood vessels developed. All of these samples will be sent to Early Path Medical Consultation Services in Larchmont, NY where they will be examined by an expert in placental pathology.

Medical Records Review: We will look at your medical records to learn more about your health and your pregnancy. We will use this information to learn more about medical conditions that you may have and tests that were done during your pregnancy. In addition, we will obtain information about your baby at delivery, including length, head size, and weight. We will primarily be looking at your medical records related to this pregnancy and birth. However, a mother's health conditions may play an

important role in pregnancy outcomes, so we will be accessing all of your medical records held at the University of Michigan Health System.

4.2 How much of my time will be needed to take part in this study?

You will be asked to participate in up to 5 study visits. The first visit will occur before you typically schedule regular prenatal care. Each visit will consist of an interview, an ultrasound of the baby, and a blood draw. The interview will typically last about 15-30 minutes. The ultrasound will last about 30-60 minutes. The blood draw will typically take about 5 minutes.

4.3 When will my participation in the study be over?

Your participation in the study will end at the time you deliver your baby, usually 6 to 8 months after you enroll in the study or if you decide to no longer participate.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks and/or discomforts associated with this study are:

Interview: Some of the questions that are asked during the interview may be personal in nature. You may feel uncomfortable answering these questions. You are free not to answer any question and you can stop the interviewer at any time.

Blood Draw: Blood drawing may cause some pain and carries a small risk of bleeding, bruising, infection at the puncture site or, rarely, fainting.

Urine Sample: There is no additional risk to you or your baby related to the collection of a urine sample.

Ultrasound: No harmful effects or medical risks have been associated with the use of ultrasonography in pregnancy to date, but this does not guarantee that none will be identified in the future. The ultrasound can occasionally suggest a birth defect when none exists. In most cases, a follow-up ultrasound exam confirms the absence of a birth defect. However, the false suggestion of a birth defect may lead you to have significant stress.

The research staff will only be looking at specific ultrasound measurements related to the size of your baby and the amount of blood it is receiving. Because of this, the ultrasound may not identify a birth defect in your baby if one exists. Please note that research staff cannot diagnose any medical conditions or release research information to you or your physician. However, if we have significant concerns about your baby's health during the study ultrasound, we may perform a formal clinical scan at the recommendation of the attending physician in the Perinatal Assessment Center. This clinical scan will become part of your medical record, and your physician will be notified of these results.

Blood Collection from the Umbilical Cord: There is no additional risk to you or your baby related to our staff obtaining a portion of the cord blood collected at delivery.

Buccal Swabs: The buccal swab may cause some discomfort and carries a small risk of bleeding at the swab site.

Microbiomics Samples: Some participants may find that the cotton salivette used to collect the saliva sample is dry and has an slightly unpleasant taste. The vaginal and anal swabs may cause minor discomfort.

Placental Samples: There is no additional risk to you or your baby related to the placental samples we collect.

Genetic analysis: There is a risk for discrimination against individuals who are at risk for a medical disorder or have a medical disorder/condition in their family. Discrimination may include barriers to obtaining health, life, or long-term care insurance, or obtaining employment. Though the different types of the VEGF gene are not definitely known to cause disease, if your genetic test results become known outside of this research, it is possible that you may experience discrimination. Extensive efforts are made to protect all research subjects from prejudice, discrimination, or uses of this information that will adversely affect them. We describe in Section 9 how you and your baby's identifiable information will be protected. It is important for you to know that few (if any) individuals who have participated in genetic studies have had any difficulty with either insurance or employment.

The research staff will only be looking specifically at genes in the VEGF family. Because of this, the genetic analysis cannot identify any known genetic disorders in you or your baby if one exists.

Research staff cannot diagnose any disease or condition based on testing that is done as part of this study. If a condition that may affect your health or the health of your baby is suspected, you will be advised to consult with your physician, who will be notified of our concerns. He or she may choose to perform diagnostic tests. If a health emergency is suspected, you will be advised to seek immediate medical care and your physician will be notified.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

You and your baby may not receive any personal or medical benefits from being in this study. Neither you nor your physician will be able to obtain the research results. One possible benefit of taking part in this study is the opportunity to receive early and more frequent pictures of your baby created by the ultrasounds. You may request printouts of these images at the time of your visit.

The results of this research and knowledge gained from it may help doctors and other health care providers identify and understand the role of various factors in maintaining a healthy pregnancy and in poor birth outcomes. We hope that this information will help promote better health and well-being for future mothers and children.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information. In addition, if new information might affect your eligibility to continue to participate in the study the researchers will inform you.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

Taking part in this study is completely **voluntary**. You do not have to participate if you do not wish. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your participation will not affect your routine prenatal care available to all expecting mothers. This usual care may involve a different frequency of ultrasounds and blood draws.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you may otherwise be entitled, including continuing prenatal care at the University of Michigan. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please notify one of the persons listed in Section 10 “Contact Information” (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

No, there will be no harm to you or your baby if you choose to leave the study before it is finished.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items, including research-related ultrasound measures and other services, that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular prenatal care
- Clinical tests required by your doctor as part of your routine prenatal care, including standard prenatal ultrasounds and any other diagnostic ultrasounds or testing that your doctor orders
- Treatment of complications
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's **medical reviewer**.

If a formal clinical scan, separate from our research study, is required during your visit, this will be billed to your health plan. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

[] _____ (check box and initial line) I understand that if an urgent or emergent condition is discovered during my research visit, my insurance company or I may be billed for clinical follow-up care that is provided to me at the time of my research visit. Such conditions may include but are not limited to:

- twin or multiple pregnancy
- ectopic pregnancy
- threatened or suspected pregnancy loss
- sub-chorionic hemorrhage
- pelvic or abdominal masses viewed on ultrasound

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

If you agree to participate in this study, you will receive a retailer gift card valued at \$10 and a parking voucher for each study visit you attend to thank you for your participation. You may also choose to have printouts of the ultrasound image of your baby at each visit.

If you decide to stop participating in this study before you have completed all study visits and procedures, you will receive the incentives for those visits that you have attended. You may keep the incentives you have already received.

8.3 Who could profit or financially benefit from the study results?

No person or organization has a financial interest in the outcome of the study.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?

To the extent possible by law, your identity and personal information provided for this study will remain confidential. However, absolute confidentiality cannot be guaranteed because of the need to give information under circumstances as described below. To protect your privacy, you will be given a unique code number that will be used instead of your name to label your research records and your lab samples. We will keep the list linking your name with your code number in a locked cabinet separate from the research records and lab samples. The research records will be kept in a research file that does not include names, medical registration numbers, or other information that is likely to allow someone other than the researchers to link the information to you. Laboratory staff performing blood, DNA, and pathological analyses will only receive coded specimens without any information that personally identifies you. All information obtained during the study, including the results of all interviews, blood tests and genetic information, will be kept confidential and any information derived from this research project that personally identifies you will not be voluntarily released by the research staff without your separate consent except:

- If necessary to protect your rights or welfare (for example, if you are injured and need emergency care)
- If required by law.

If the researcher orders any clinical tests in consultation with your physician, the order and results may become part of your regular medical record.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Your AIDS/HIV status
- All records relating to your pregnancy, the treatment you have received, and your response to the treatment
- Billing information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
 - Make sure the study is done safely and properly
 - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article or presented at a scientific meeting, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over. Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan Notice of Privacy Practices. This information is also available on the web at <http://www.med.umich.edu/hipaa/npp.htm>. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Sample Repository. Researchers in the GROW study are dedicated to improving the health of women and children. The data, tissue, blood and samples from your body collected during this study are important to this study and to future research. With your consent, remaining blood, DNA, and placental samples from this study will be kept in a laboratory repository for an indefinite period of time. All personally identifying information will be removed from these samples. They will be identified only by the study code number. We may use these samples in the future blood and DNA analyses in our ongoing research related to the influence of genes and other factors on placental development, fetal growth, birth outcomes, and child health. We may share these samples and research data with other scientists not at the University of Michigan, but we will not give them any information that would personally identify you. We will not put the results of any tests conducted on these samples in your medical record.

_____ (check box and initial line) **I AGREE** to allow the study investigators to keep my samples in a repository for these future studies.

_____ (check box and initial line) **I DO NOT AGREE** to allow the study investigators to keep my samples in a repository for these future studies.

9.4 When does my permission expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

Study investigators may conduct further studies based on the results of this study. In that case, the study investigators may want to contact you at some time in the future to ask follow-up questions and/or discuss whether you would be interested in participating in these future studies. If you consent to future contact, information for identification, eligibility, and contact for future studies on placental development, fetal growth, and birth outcomes will be kept in a study registry separate from our research database.

_____ (check box and initial line) **I AGREE** to allow the study investigators to contact me in the future to ask follow-up questions and/or discuss my interest in participating in these future studies.

[] _____ (check box and initial line) **I DO NOT AGREE** to allow the study investigators to contact me in the future to ask follow-up questions and/or discuss my interest in participating in these future studies.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Vinod K. Misra, MD PhD
Mailing Address: D5257 Medical Professional Building
1500 E. Medical Center Drive
Ann Arbor, MI 48109-0718
Telephone: (734) 615-3108

Study Coordinator: Sheri Trudeau, MPH
Mailing Address: D5257 Medical Professional Building
1500 E. Medical Center Drive
Ann Arbor, MI 48109-0718
Telephone: (734) 615-3108
Email: growstudy@umich.edu

You may also express a concern about a study by contacting the Institutional Review Board listed below, or by calling the University of Michigan Compliance Help Line at 1-888-296-2481.

University of Michigan Medical School Institutional Review Board (IRBMED)
Argus I
517 W. William
Ann Arbor, MI 48103-4943

Telephone: 734-763-4768
Fax: 734-615-1622
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy, contact the University of Michigan Health System Privacy Officer at 1-888-296-2481.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. *(Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Signature of Subject: _____ Date: _____

Name (Print legal name): _____

Date of Birth: _____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____