Consent Form

Title of Research Study: The effect of inflammation and damage to lymph node structures on durable protective immunity following yellow fever vaccination

Investigator Team Contact Information: Timothy Schacker, MD

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

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Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you are a healthy adult. You are planning to receive the yellow fever vaccine for upcoming personal or business travel and you expressed interest in participating in this study.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

How well a vaccine works sometimes varies by geography, with good protection in one part of the world and poor protection in others. In this research study, we want to find out if this difference is because of different infections in communities, which could affect parts of the immune system that are needed for a good response to a vaccine.

In this study, we will give the yellow fever vaccine to healthy participants in Uganda and Minnesota, and compare levels of infections (from viruses, bacteria, fungi, parasites, and helminths [a type of parasitic worm]) in these participants. This will help us learn more about relationships between these infections, how they affect your immune system, and how that affects your body's response to a vaccine.

How long will the research last?

We expect that you will be in this research study for 21 visits over 18 months (a year and a half).

What will I need to do to participate?

You will have a lymph node biopsy, and have leukapheresis (a procedure to remove some white blood cells from your blood, described in detail below), both before and after you are given a yellow fever vaccine. If you are not eligible or unable to tolerate leukapheresis, a large volume blood draw (60 cc, or about 4 tablespoons) will be drawn. The yellow fever vaccine will be administered at a travel clinic and you or your insurance company will pay for the clinic visit and vaccine costs. You will be asked to return for all study visits and to follow instructions given to you by the study team.

The yellow fever vaccine is safe and effective. It usually provides life-long immunity against yellow fever. The vaccine is a live, weakened form of the virus given as a single shot. The vaccine is recommended for people aged 9 months or older who are traveling to or living in areas at risk for yellow fever virus in Africa and South America. Normally, Minnesotans would only receive this vaccine if they were going to travel or live in these areas.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

Common side effects associated with the yellow fever vaccine include:

- Redness and pain at the injection site
- Headache
- Fever
- Muscle aches

- Malaise (general feeling of being unwell)

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?
We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits to society include learning more about how to make vaccines work better.

What happens if I do not want to be in this research?
You do not have to participate in this research if you do not want to.

Detailed Information About This Research Study
The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?
We expect about 16 people in Minnesota will participate in this research study, and 30 people in Uganda will participate in this study, for a total of 46 people enrolled internationally.

What happens if I say "*Yes, I want to be in this research*"?
If you agree to participate in this study, you can expect the following procedures and visits. During the COVID-19 pandemic, you will be screened for COVID-19 symptoms before coming to any in-person visits.

Procedures:

Leukapheresis:

Leukapheresis is a procedure used to remove and isolate a large volume of white blood cells from your blood so that they can be studied in the lab. The procedure involves passing your blood through a machine that collects white blood cells from your blood. The rest of your blood is returned to your body. Needles will be placed in both of your arms, one where your blood is removed and one where the blood returns to your body. The procedure will take approximately 4 hours.

** If you are not eligible or unable to tolerate leukapheresis, a large volume blood draw (60 cc, or about 4 tablespoons) will be drawn.

Lymph node biopsy:

Lymph node biopsies of your groin will be done at the research clinic. The actual surgery will only take 30-40 minutes but you will need to be there at least 6 hours. You should not eat or drink anything for at least 6 hours before the biopsy. The groin area will be scrubbed with an antiseptic solution. Local anesthetics (similar to Novocain) will be injected to numb the area. An incision that is approximately 1 – 3 inches long will be made. The lymph node will be uncovered and removed. A lymph node is about the size of a peanut. The surgeon will close the wound with stitches, and then a bandage will be put over the wound.

After a period of at least 4 hours you will be allowed to go home. You will be asked to remain inactive until the next morning. You and the surgeon will discuss the use of a drug to relieve any pain. The entire procedure from the time you enter the hospital until you are discharged should be no longer than 8 hours.

After the procedure, you may be examined in the research unit if you are experiencing any complications

from the procedure. The wound will be examined and you will be asked questions about pain, drainage from the wound, or discomfort. If there is any sign of infection you will be referred back to the surgeon for another examination and a prescription of antibiotics or another appropriate treatment. The exact antibiotic will be chosen by the surgeon or investigator.

The surgeon will advise you as to the best way to manage stitches that are in place. They may ask you to come back to clinic 5-7 days after the procedure to have the stitches removed, or the stitches may be the dissolving type. You will be fully informed of which type you have.

Visit Schedule (please also see the table at the end of this consent form)

Screening (Day -42 to 1)

- You will discuss this consent form with the study team and, if you are interested, sign the form before any research procedures take place
- You will have a blood draw
- If you are a woman who can have children, you will have a pregnancy test

Leukapheresis Screening

- You will discuss the leukapheresis procedure with an MD
- Your veins will be examined to see if you are a good candidate for the procedure
- You will be asked about your medical history

Baseline (Day -35 to1)

- You will have a physical exam, including your height and weight
- The study team will ask you about your medical history
- You will undergo leukapheresis
    - If you are not eligible or unable to tolerate leukapheresis, a large volume blood draw (60 cc, or about 4 tablespoons) will be drawn.
- If you are a woman who can have children, you will have a pregnancy test prior to leukapheresis
- You will have a lymph node biopsy
- You will have stool and urine collected
- You will have a blood draw of 15cc of blood.

Day 1

- You will receive the yellow fever vaccine from a travel clinic

Day 3, 5, 7, 10, 12, 14, and 17

- You will have a blood draw
- At Day 10, you will provide a stool sample
- At Day 7 and Day 17, if you are a woman who can have children, you will have a pregnancy test
  **At Day 17, you will have a research blood draw of 60 cc of blood

Week 3

- You will have a blood draw
- You will have a lymph node biopsy
- If you are a woman who can have children, you will have a pregnancy test

Week 4, 6, 8, 10 and 12:

- You will have a blood draw
- At Week 4, you will provide a stool sample. If you are a woman who can have children, you will have a pregnancy test
- At Week 12, we will collect a stool and urine sample from you

Month 6, 9, 12, and 15:

- You will have a blood draw
- At Month 6, you will have stool collected
- At Month 6, you will also undergo leukapheresis
    - If you are not eligible or unable to tolerate leukapheresis, a large volume blood draw (60 cc, or about 4 tablespoons) will be drawn.
    - If you are a woman who can have children, you will have a pregnancy test prior to leukapheresis
- At Month 12, we will collect a stool and urine sample from you

Month 18 (Final Study Visit)

- We will collect a stool and urine sample from you
- You will have a blood draw

What happens if I say "Yes", but I change my mind later?

You can leave the research study at any time and no one will be upset by your decision.

If you decide to leave the research study, contact the investigator to let him know.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future medical care.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

This study has the following risks:

Yellow Fever Vaccine (standard of care at a local travel clinic):

Reports of serious side effects to yellow fever vaccine are extremely rare and generally include fever, headache, and muscle ache. The current estimates of the risk from yellow fever vaccination are below. Please talk with the provider at the travel clinic if you have any questions.

- most people will get sore at the site of injection,
- 2-10% may feel tired, experience headache experience muscle aches, and/or have a fever for 24 hours starting 3-9 days after vaccination,
- Out of 130,000 vaccine recipients, 1 may get immediate hypersensitivity – rash, itching, faintness, or asthma – this is why you need to wait at least 30 minutes in the clinic after receiving the vaccine.
- 1 to 25 in 10 million vaccine recipients may experience inflammation of multiple organs e.g. lungs, kidney, liver, spleen, skin, blood stream.
- 1 in 8 million will get encephalitis (inflammation of the brain). There have been a few deaths

reported from the more serious side effects of the vaccine, but this seems more common in those over 70 years age.

Lymph node biopsy:
The risks of the lymph node biopsy are

- bleeding
- infection
- seroma (a pocket of clear fluid that sometimes develops)
    - Any participant who develops a seroma could have it drained with a syringe in the clinic. However, it is unlikely that a seroma would need to be drained. The risks of draining a seroma include pain, infection, or that the seroma could come back. These risks are very low.
- scarring

You will be observed in the research clinic before you are allowed to go home. If you develop complications, care will be provided to you.

Leukapheresis:
The risks of the apheresis process include

- bruising and/or bleeding in the arms when needles are placed for the apheresis
- a reaction to the drug used to prevent your blood from clotting during the procedure
- loss of blood, especially platelets

Rarely, veins cannot be found to insert the needles, so a catheter must be placed in a large neck vein to collect the cells.

Stool Collection Risks
You may find it distasteful to collect and mail and/or store stool until your study visit.

Blood draw:
Events associated with venipunctures include

- discomfort
- slight bruising
- bleeding
- lightheadedness
- fainting
- rarely, infection at the venipuncture site

What do I need to know about reproductive health and/or sexual activity if I am in this study?

Female volunteers should not get pregnant during the study because vaccine effects to the embryo/fetus are unknown. If you are a woman of childbearing potential, you must use contraception for one month following the vaccine.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you. If a test result indicates you may

need follow-up care with your primary physician, that care will be billed as usual, to you or your insurance. In addition, the costs related to the yellow fever vaccine will be your responsibility to cover.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance.

Certificate of Confidentiality

To help protect your privacy, the National Institutes of Health has granted a Certificate of Confidentiality. The researchers can use this Certificate legally to refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate does not prevent a researcher from reporting information learned in research when required by other state or federal laws, such as mandatory reports to local health authorities for abuse or neglect of children/vulnerable adults, or information to the Food and Drug Administration (FDA) when required in an FDA audit. However, the Certificate limits the researcher from disclosing such information in follow up civil, criminal, legislative or administrative legal proceedings if the information was created or compiled for purposes of the research.

You also 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, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

What will be done with my data and specimens when this study is over?

Your data and/or samples (include as applicable) will not be used for any future research after this study is complete.

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

Will anyone besides the study team be at my consent meeting?

You may be asked by the study team for your permission for an auditor to observe your consent meeting (or a recording of your consent meeting). Observing the consent meeting is one way that the University of Minnesota makes sure that your rights as a research participant are protected. The auditor is there to observe the consent meeting, which will be carried out by the people on the study team. The auditor will not document any personal (e.g. name, date of birth) or confidential information about you. The auditor will not observe your consent meeting (or a recording of your consent meeting) without your permission ahead of time.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 or go to https://research.umn.edu/units/hrpp/research-participants/questions-concerns. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Can I be removed from the research?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include

- If you become pregnant before the vaccine is administered or 30 days after the vaccine
- If you do not follow the instructions of the study team
- If the study doctor determines that the study is not in your best interest
- If you become infected with HIV

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

If you agree to take part in this research study, you will be compensated as follows. If you complete all study visits, this is a total of up to $2,300 for the entire study:

- Screening: $50
- Leukapheresis consult: $50

- Leukapheresis : $300
    - If you are not eligible or unable to tolerate leukapheresis, a large volume blood draw will be drawn and you will be compensated $50.
- Baseline: $600
- Day 3, 5, 7, 10, 12, 14, 17 and Week 4, 6, 8, 10, 12 and Month 6, 9, 12, 15: $25
- Week 3 biopsy: $600
- Month 6 leukapheresis: $300
    - If you are not eligible or unable to tolerate leukapheresis, a large volume blood draw will be drawn and you will be compensated $50.

Payment you receive as compensation for participation in research is considered taxable income. If payment to an individual equals or exceeds $600 in any one calendar year, the University of Minnesota is required to report this information to the Internal Revenue Service (IRS). Research payments to study participants that equal or exceed $600 during any calendar year will result in a FORM 1099 (Miscellaneous Income) being issued to you and a copy sent to the IRS.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Signature Block for Capable Adult:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent