INSTITUTE: National Institute of Allergy and Infectious Diseases

STUDY NUMBER: 18-I-0139 PRINCIPAL INVESTIGATOR: Matthew J. Memoli MD, MS

STUDY TITLE: Defining Skin Immunity of a Bite of Key Insect Vectors in Humans

Initial Review Approved by the IRB on 08/10/18
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Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

PURPOSE OF THE STUDY

Diseases spread by insects continue to cause significant health problems and deaths worldwide despite ongoing efforts to control them. Mosquitoes can spread viruses like dengue, yellow fever, West Nile virus, chikungunya, Rift Valley fever, Japanese encephalitis, and Zika virus. Some mosquitoes and similar insects called sand flies carry parasites that can cause diseases like malaria and leishmaniasis. These viruses and parasites can spread quickly and can be difficult to control.

The way people's bodies respond to mosquito or sand fly bites may affect how people get infected with these viruses and parasites. The body's response to insect bites is caused by the immune system, which is the part of the body that helps fight off infections. In this study, we want to understand how the immune response in your skin responds to mosquito or sand fly bites. We also want to understand how the immune response in your skin changes after you are bitten on multiple days. Understanding how the skin responds may help researchers develop better vaccines in the future. We plan to enroll about 90 people in this study. We will take mosquitoes or sand flies that are raised in a laboratory and let them bite participants on the arm during "feeding" sessions. These mosquitoes and sand flies do not carry any diseases and cannot give you any diseases. Then we will take blood and biopsies of participants' skin to use for research tests.

Participants in this study will be divided into 2 groups (cohorts) depending on their availability, screening blood test results, and the cohorts that we are filling at the time. If you enroll in Cohort A, your time in the study will be about 1 week. If you enroll in Cohort B, your time in the study will be about 8 weeks.

CRITERIA TO TAKE PART IN THIS STUDY

You are being asked to participate in this study because you are a healthy adult who meets the age requirement and has completed the screening process. You may participate if you:

- meet all of the study requirements,
- are willing to have your samples stored for future research,
- agree to not use scented lotions, deodorants, or topical creams on each feeding day,
- agree to not take aspirin or any other NSAID within 7 days of a biopsy,
- agree to not use topical steroid creams or ointments (for example: hydrocortisone) throughout the study unless discussed with the study team, and
- agree to all of the study procedures described below.

If you are female, you cannot be in this study if you are breastfeeding or pregnant. Additionally, you must not become pregnant during this study. This means you must be postmenopausal or surgically sterile, abstain from reproductive sex, or use contraceptives. Adequate contraception is condoms with spermicide worn by males plus a form of contraception used by females. This includes an intrauterine device, a diaphragm, or form of contraception that is oral, injected, or implanted. Women must use contraceptives for 4 weeks before starting the study and continue using them until the end of the study.

Participation in this study is entirely voluntary. Declining to participate in this study will in no way affect your relationship with the NIH or the NIH staff.

STUDY PROCEDURES

The study will take place in the Clinical Center (CC) on the NIH campus in Bethesda, MD. If you decide to join, you will have the following procedures and tests done throughout the study. A member of the study staff will explain the schedule and let you know how often each procedure will be performed.

Cohort A	
Day 0	Medical history, exam, mosquito or sand fly feeding, skin punch biopsy X 3 (visit lasts about 6 hours), blood draw
Day 1 (+1 day)	Biopsy assessment and blood draw X 1 (visit lasts about 1-2 hours)
Day 7 (±3 days)	Telephone call follow-up
Cohort B	
Days 0, 14, and 28 (±7 days)	Medical history, exam, mosquito or sand fly feeding (visits last about 1-2 hours each), blood draw (Day 0 only)
Day 42 (±7 days)	Medical history, exam, mosquito or sand fly feeding, skin punch biopsy X 2 (visit lasts about 6 hours)
Day 44 (+3 days)	Medical history, exam, blood draw X 1, skin punch biopsy X 1 (visit lasts about 1-2 hours)
Day 51 (±3 days)	Telephone call follow-up

Medical History: We will review your medical history with you, including medications you are taking now and have taken recently.

Physical Exam: We will perform a complete physical examination including blood pressure, heart rate, respiratory rate, temperature, weight, and finger-measured oxygen level.

Blood Draw: A blood draw involves using a needle to remove blood from your vein. We will collect blood at two visits (per cohort). We will use the blood to study how your immune system responds to the insect bites. We may also store some blood for future research tests.

The amount of blood drawn during the study is approximately 7 tablespoons of blood over the entire length of the study. This amount is within the limits allowed by the NIH CC for research purposes. While in the study, please tell the study staff if you are participating in other studies or will have blood drawn for any other reason including blood tests or blood donation.

Urine Collection: For women who can become pregnant, we will collect your urine for a pregnancy test before each insect feeding.

Mosquito or Sand Fly Feeding: At each feeding, 5 to 10 mosquitoes or sand flies will be allowed to bite your arm through a feeding device for up to 20 minutes. If you are in Cohort A, you will undergo 1 mosquito or sand fly feeding. If you are in Cohort B, you will undergo 4 feedings, each about 2 weeks apart (with a minimum of 7 days in between feedings). If the mosquitoes or sand flies do not feed or fed poorly (for example: only 1-2 insects fed), you may undergo a repeat feed immediately after with 5-10 fresh insects. The insects are grown at the NIH in a controlled environment, so they do not carry any diseases and cannot give you any diseases.

Skin Punch Biopsy: We will take a total of 3 small skin punch biopsies from your arms throughout the study. This is a routine procedure that takes about 5-10 minutes. We will take two from the skin where you were bitten and one from skin without any bites on the opposite arm. After we clean the skin with alcohol and/or a topical antiseptic, we will inject a medicine to numb your skin at the biopsy site. A sharp tool that looks like a small cookie cutter will be used to remove a round piece of skin that is slightly smaller than a pencil eraser. A dressing will then be applied to the site. You must keep the dressing over the biopsy site dry for 1 to 2 days, and change it as needed for about a week. If we sew the biopsy site with stitches, the study doctor will take them out after about 10 days.

If you are in Cohort A, you will have three skin biopsies on Day 0 after the feeding. If you are in Cohort B, you will have three skin biopsies after the fourth feeding; two on Day 42 and one on Day 44. We will use the skin biopsies to study how your skin changes after insect bites.

Phone Call: A member of the study team will call you approximately 7 days after the last insect feeding and biopsy to see how you are doing and to see if you have any redness or discomfort from the bites or the biopsy.

RISKS

Risk of Mosquito or Sand Fly Feeding: You may have some itching, mild rash, or irritation where the mosquitoes or sand flies bite you. Applying cold packs and administering over-the-counter pain medications or antihistamines (topical or oral, such as diphenhydramine or Benadryl®) if necessary can generally treat these reactions. You may have scarring such as darkening of your skin where mosquitoes or sand flies bite you or from scratching after the mosquitoes or sand

flies bite you. You may need to put some medicated cream or lotion on the area or take an oral medication if it bothers you. Rarely, mosquito or sand fly bites can cause more severe irritation, severe allergic reactions leading to shock that requires immediate treatment, or infections at the site of the bite requiring antibiotics. If you have an infection at the site of biting that requires antibiotics, we will treat you.

Risk of Skin Punch Biopsy: You may have pain or discomfort during and after the biopsy, even with the numbing medicine. You may feel some mild burning when the numbing medicine is injected into the skin. Injecting the numbing medicine can also cause bruising, skin irritation or, rarely, an allergic reaction, which can be treated. You may have minor bleeding or redness at or around the biopsy site. A skin biopsy will result in a scar at the site, and we cannot tell what the scar will look like ahead of time. There is a chance that the scar will become raised and hard, which is called a "keloid." If this occurs, a dermatologist may be able to help soften and flatten the scar, but this may be permanent. Although rare, it is possible for the biopsy site to become infected. If you get an infection, we will treat the infection with antibiotics, if necessary.

Blood Draw Risk: Drawing blood may cause pain, bruising, lightheadedness, dizziness, possible fainting, local discomfort, bleeding, and, rarely, infection or blood clot where the needle was inserted.

POTENTIAL BENEFITS

You will not receive any direct medical benefit for participating in this study. However, what we learn from this study may allow us to further develop a new vaccine for mosquito-borne infections that may benefit others in the future.

ALTERNATIVES TO PARTICIPATION IN THIS STUDY

You may choose not to participate in this study. This will not affect your eligibility to participate in other protocols at the NIH.

USE OF RESEARCH DATA

To advance science, it is helpful for researchers to share information they get from studying human subjects and their data. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the information combined from many studies to learn even more about health and disease.

If you agree to take part in this study, some of your data will be placed into one or more scientific databases after it has been stripped of identifiers such as name, address, and birth date. It may then be used for future research on any topic and shared broadly for research purposes. A researcher who wants to study the information must apply for access to the database. Researchers who are approved to access the database may be able to see and use your information, along with information from many other people. You will not receive direct benefits from future research that uses your data and information.

WITHDRAWAL FROM THE STUDY

You may voluntarily withdraw from this study at any time and withdraw permission for your individual data, specimens, and health information to be used for additional or future research. If you choose, you may request to have your research data destroyed. However, it may not be possible to withdraw or delete data once they have been shared with other researchers.

Additionally, you may be removed from the study without your consent if the study team feels it is in your best medical interest, if the research is stopped, or if you do not follow study requirements. If you leave the study prior to completion, you may be asked to come in for a final study visit.

If you become pregnant, study procedures will be stopped, but, with your permission, we will continue to follow you for protocol related safety issues until your delivery.

COSTS TO YOU FOR YOUR PARTICIPATION IN THIS STUDY

There will be no charge to you or your health insurance company for any tests, procedures, or medications directly related to this study.

COMPENSATION

You will be compensated in accordance with CC guidelines for compensation of healthy volunteers. The compensation will be determined considering your time and the inconvenience of participating in this study, and will also be based on the number of clinic visits and the number of days you participate in the study. The compensation plan is listed below:

Cohort A	
Day 0	$825
Day 1 (+1 day)	$100
Expected total for completing ALL Cohort A study visits	***$925***
Cohort B	
Day 0	$325
Day 14 (±7 days)	$425
Day 28 (±7 days)	$425
Day 42 (±7 days)	$725
Day 44 (+3 days)	$200
Expected total for completing ALL Cohort B study visits	***$2100***
Investigator-requested interim visits	$75

The total expected compensation is $925 for Cohort A and $2100 for Cohort B if you complete all study visits as planned. You will be compensated according to the number of visits that you complete. If you are in Cohort A, compensation will be processed after the phone call on day 7. If you are in Cohort B, compensation will be processed in two parts; after the day 28 visit and after the phone call on day 51. Please note that compensation may take up to 2-3 weeks or longer to receive.

If deemed medically necessary by the doctor, you may be asked to come in for additional follow-up visits. Reimbursement will be provided for interim visits that are requested by the Principal Investigator, but not for interim visits requested by the participant.

STORED SAMPLES AND DATA AND FUTURE RESEARCH

If you agree to participate in this study, you also agree to let us store your samples and data for future research. These stored samples and data may help us learn more about the immune response to mosquito and sand fly bites. We will label your stored samples and data with a code that only the study team can link to you. We will keep any information that can be traced back to you as private as possible. If you change your mind and decide you do not want us to store your samples and/or data, please contact us. Samples and data collected prior to this request will be stored and used as described above. However, if you specifically request to remove all of your samples from the study, we can destroy stored samples. We cannot delete data that have already been shared or remove documents from your NIH medical record.

We may send your coded samples and/or data to other investigators for their research. We might also share information such as your sex, age, health history, or ethnicity. We will not sell your samples or data and you will not be paid for any products that result from the research. Future studies may need health information (such as smoking history or present health status) that we don't already have. If so, our study team will contact you. Future research that uses your samples and data will probably not help you, but it may help us learn more about health and disease. In general, the research tests we perform are not like routine medical tests, and may not relate directly to your medical care.

The greatest risk associated with storing samples is that someone may take information from your medical records without your permission. The chances of this happening are very low. If this information becomes available, you may face discrimination when you apply for insurance or a job. You may also have similar problems if you share the information yourself or let us release your medical records.

NEW FINDINGS

Any new findings that are discovered during this study, including those that may affect your willingness to continue, will be fully discussed with you.

CLINICALTRIALS.GOV

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

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Matthew J Memoli, M.D., M.S., at Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, MSC 3203 33 North Dr., Bethesda, MD 20892, through the study team at 301-594-0803, 301-761-6800 or by email: holly.baus@nih.gov.

You may also call the Clinical Center Patient Representative at (301) 496-2626.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/Legal Representative _____ Date _____

Print Name _____ Time _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM AUGUST 10, 2018 THROUGH AUGUST 9, 2019.

Signature of Investigator _____ Date _____ Signature of Witness _____ Date _____

Print Name _____ Time _____ Print Name _____ Time _____