



CTC/ WRAIR
503 Robert Grant Avenue, Room 2W78
Silver Spring, Maryland 20910
Telephone: 301.319.9660
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WRAIR study #1584, Principal Investigator Dr. Spring:

This study is researching malaria vaccines.

Malaria is a disease that can range from mild illness to death. Humans get this disease by being bitten by mosquitoes that are infected with malaria parasites. While not found in America, it is in places such as Africa, Asia and Latin America. There are 300 – 500 million clinical cases and 1-2 million deaths annually. Ways to prevent getting sick with malaria include avoiding mosquitoes (using screens on windows, using bed nets or wearing insect repellent) or taking medicine once a day or once a week in order not to become sick. But a vaccine to protect against malaria, much like a flu vaccine protects against flu, would be beneficial both to people living in, or traveling to, areas where it is commonly found.

The site for this study is the Clinical Trials Center (CTC) at the Walter Reed Army Institute of Research (WRAIR) here in Silver Spring, Maryland. The organization we are working with, who designed the vaccine, is called Seattle Biomedical Research Institute (SBRI). The name of the doctor heading up the study is Dr. Michele Spring who works at WRAIR. During the trial, you may meet other investigators who are helping run the study as well as the staff of the CTC.

In the life cycle of the malaria parasite, a mosquito, carrying the malaria organism, bites a human and injects the parasite into the skin. Then the parasite moves to the liver, where it multiplies greatly. The person does not know he/she is carrying the malaria parasite at that time. Then after about 7-10 days, the malaria parasite enters the bloodstream and starts to invade red blood cells and multiply within the body. This is when the human feels very sick. He/she can develop flu-like symptoms at first (fever, body aches, headache, chills, sweats, fatigue etc) but then if the infection is not treated, many red blood cells can be destroyed causing anemia, and all body systems can start to malfunction (like liver and kidney failure), eventually leading to coma, and even death. When the parasite is circulating in the blood, a scientist can take a sample of blood and looking under the microscope, see the malaria parasite. This is how we diagnose malaria. Then anti-malaria medications can be given to cure the disease.

Vaccine Information:

The experimental vaccine is called GAP- which stands for genetically attenuated parasite. What this means is that researchers have taken the malaria parasite and changed it so that it cannot fully develop. So when you give the GAP vaccine to a person, the body thinks it is “seeing” malaria and thus develops an immune response against it. Since the malaria parasite has been altered, it doesn’t go on to cause disease. Then if the person were to travel to an area and get “real” malaria, the body would already have defenses against it. This type of vaccine is the same type of vaccine used for measles or chicken pox and the nasal flu vaccine.

Since we are giving the whole malaria parasite as a vaccine, we would like to give it the same way it is given in nature - by mosquito bite. Someday, we will be able to give it by injection or another method, but at this time, we are testing it with mosquitoes.



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In the secure insectary at WRAIR, we have mosquitoes that have never been out of the insectary. We can have these mosquitoes take up the GAP (the altered malaria organism). Then we will have the GAP-infected mosquito bite you. This will inject the GAP product in- much like regular vaccine. The GAP can go from the skin to the liver but because it is has be altered by researchers, it cannot grow and multiply in the liver. That means that the malaria organism will not develop to enter the bloodstream- and no clinical signs/symptoms of malaria will develop.

The vaccine is not licensed by the FDA; which means it is experimental and has FDA approval to undergo testing like in this study. The vaccine has been made under conditions acceptable to the FDA. This vaccine has been tested in mice and has been found to be safe.

Giving a malaria vaccine by mosquito bite has been done before at WRAIR. In these instances, the malaria parasite was put into mosquitoes and then put underneath x-rays. (The x-rays changed the parasite so it could not fully develop in humans.) The mosquitoes bit the human volunteers and thus transferred the altered malaria parasite to volunteers. Later, the volunteers were given malaria. A very large percentage of theses volunteers were protected- meaning they never got sick. We believe their immune system recognized and eliminated the wild type malaria because they had seen an altered form of malaria previously. Several studies like this one showed that volunteers needed to be bit by at least 1000 x-rayed mosquitoes be protected. We will also aim to have 1000 bites. To get to this number of bites, we are aiming to have 200 bites per session with a total of six sessions. We may find we need more if after 6 sessions we don't get > 1000 bites. We will be showing you a short video on how the bites are given.

Goals of the Study:

1. To see if a new investigational malaria vaccine is safe.
2. Some volunteers will be involved in the part of the study to see if these vaccines either prevent or postpone malaria.
3. In all volunteers, we will be looking to see how their immune system reacts to the vaccine.

Number of people in the study:

We will be testing a low dose of one vaccine in a small group of volunteers first.

Group 1: 6 volunteers.

Group 2: 20 volunteers

Control Group: 6 volunteers

We will have alternates- which are volunteers who will step in if a regularly scheduled volunteer is unable to participate.

Study Process

1. Screening Phase:

In depth explanation of the study by a study investigator

Informed consent review and signing



Comprehension assessment by written test, with review as needed
Brief medical history, medical exam, and blood testing

2. Immunization Phase:

There are two groups. The first group received two vaccinations; the first contained five mosquitoes, and the second 200 mosquitoes, approximately one month apart.

We are now recruiting for Group 2:

In each vaccination, we want to have a total of 200 mosquitoes bite you. Each of these mosquitoes will contain GAP – the altered malaria parasite. The mosquitoes will bite your forearm for 5 minutes. Possible side effects of the immunizations are redness, swelling and/or itching at the site due to mosquito bites. With a goal of 200 mosquito bites, we know that when we place the mosquitoes on your arm, not all of them will bite. So we will place more than 200- about 300- in the cartons. That way even if a large percentage chooses not to feed, we believe we will achieve about 200 bites. We will show you a short video on how this procedure is done.

What we anticipate is that the GAP will be passed from the mosquitoes, into your skin and to the liver, where it will not be able to develop and thus disappear.

A first group of volunteers will have already undergone this type of vaccination. We will only do this part of the study if the vaccine was safe and never reverted back to wild type form. We will follow you with regular clinic visits to make sure you continue to feel well and don't have signs of malaria. We will aim for > 1000 bites, therefore 6 immunizations, given at approximately 1 month apart. We have a schedule attached to the informed consent form.

Malaria symptoms may include a fever, headache, fatigue, vomiting, diarrhea, muscle aches, and / or stomachache. If you do develop malaria at any time, the strain used in this study is very sensitive to a drug called chloroquine. This is an oral drug that you take for three days. This drug has few side effects, which may include an upset stomach, nausea, and/or diarrhea.

Infectivity Controls:

This small group of 6 volunteers will be enrolled to ensure that our malaria challenge model works and to provide a comparison group to the vaccinees. These volunteers will undergo malaria challenge, and **WILL BE EXPECTED CONTRACT MALARIA FROM THE MOSQUITO BITE**. They will undergo all the procedures described for the Challenge Phase, but once they contract malaria in the hotel, they will be treated with chloroquine and released from the hotel. They will come to four weekly visits and the final 3-month post-challenge visit.

3. Challenge Phase:

There are no blood tests to see if the vaccines are effective. In order to test if they are effective against malaria, once the immunization phase of this study is over, you will undergo a challenge against malaria.

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- The challenge entails being bitten by a mosquito that is infected with malaria in a carefully controlled setting here at Walter Reed. **YOU MAY CONTRACT MALARIA FROM THE MOSQUITO BITE.**
- The strain of malaria used in this study will not recur after treatment.
- **Hotel Phase:**

Approximately six days after the challenge, we will need to see you in the Clinical Trials Center during which you will have a small amount of blood drawn to check for malaria.

Malaria symptoms may include a fever, headache, fatigue, vomiting, diarrhea, muscle aches, and / or stomachache.

Then, at approximately day 9 through day 20 after challenge, all volunteers and study staff will check into a local area hotel. This is done to offer the fastest available assessment and treatment if needed.

During the hotel phase, you can come and go for work or outside activities, but we ask that you sleep at the hotel. That way, for example, if you didn't feel well during the night, you wouldn't have to wait for the clinic to open; you would be seen immediately.

If you do develop malaria at any time, the strain used in this study is very sensitive to a drug called chloroquine. This is an oral drug that you take for three days. This drug has few side effects, which may include an upset stomach, nausea, and/or diarrhea.

Once treated, you would then be monitored weekly for four weeks in a row and complete the study.

Again, the strain of malaria used in this study will not recur after treatment.

If you develop malaria, you will not be able to donate blood for three years.

If you do not become positive for malaria during the hotel stay, you will be checked daily at the Clinical Trials Center to day 31 post-challenge (excluding weekends / holidays if corroborated by investigator). After that, we will check you weekly for four weeks in a row, with a 3-month post-challenge visit.

If you are protected from malaria completely, meaning the vaccine worked, we will invite you to take part in another malaria challenge 6 months after the first one. The same exact procedures will apply, with a 3- and 6-month post-challenge visit.

Duration:

Group 1: Participation may be up to 9 months (3 months screening, 6 months study participation). Note: this group is closed to enrollment.

Group 2: Participation may be up to 17-23 months (3 months screening, 6 months immunization, and depending upon protection of vaccine, 4-7 months challenge, and 4-7 months rechallenge).

Control Group: Study participation - up to 6 months (3 months screening and 3 months challenge)



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Brief overview of Inclusion criteria:

Healthy adult, 18 – 50 years of age,
Male or female, military or civilian,
Not receiving any other investigational products,
If female, no plans to get pregnant and using successful method of birth control as outlined in informed consent

Brief overview of Exclusion criteria:

History of malaria or known exposure to malaria,
Allergy to components mosquito bites,
HIV, immunodeficiency diseases (cancer, transplant patient)
Chronic significant heart, kidney, neurological or liver disease,
Pregnancy or planned pregnancy,
Use of certain prescription medications,
Any other significant finding that in the opinion of the investigator would increase the risk of having an adverse outcome from participating in this study.

Approximate compensation breakdown:

Screen - \$25.00
For the Immunization Phase, payment is \$100.00 for each blood draw, excluding unscheduled clinical labs drawn. During the hotel phase, the hotel room is paid for by us.
Group 1- \$5000
Group 2 -\$6500 for Immunization Phase and first challenge; \$3300 for rechallenge
Challenge control cohort – \$1700-\$2200, depending on when they become ill with malaria