PRINCIPAL INVESTIGATOR: [redacted]

STUDY TITLE: An Investigation of Vitamin A Palmitate Supplementation in Patients with Reticular Pseudodrusen (RPD) and Delayed Dark Adaptation

STUDY SITE: NIH Clinical Center

Cohort: Standard

Consent Version: July 25, 2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator

[redacted]

Study Coordinator

[redacted]

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are

being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

PURPOSE OF THIS STUDY

Macular degeneration is a condition that can cause permanent loss of central vision, which is important for seeing fine details and tasks such as reading, driving or sewing. Age-related macular degeneration (AMD) is the leading cause of vision loss in people over 55 in the United States. Changes in the eye can lead to difficulty with adjustment of the eye to low light, known as dark adaptation.

Identifying and watching the early to intermediate stages of AMD and changes in dark adaptation may help us develop new treatments to stop the disease before it becomes severe. The purpose of this study is to see if taking 16,000 IU of vitamin A per day could improve vision in people with reticular pseudodrusen (RPD) in Cohort 1 and if an increased dosage of 48,000 IU of vitamin A per day could improve vision in people with RPD in Cohort 2. A procedure that measures how your eyes adjust to the dark (dark adaptation protocol) can be used to identify and monitor RPD. We are also doing this study to improve our understanding of RPD and associated dark adaptation.

BACKGROUND

A first step in understanding the disease would be to watch people who have been taking vitamin A. Previous researchers have shown that taking vitamin A could help improve vision. However, further research is needed to fully understand these changes.

STUDY POPULATION

You have been asked to participate in this study because you have been diagnosed with RPD. Up to 18 people with RPD may participate in this study. Eight participants were enrolled in Cohort 1 and up to 10 participants will be enrolled in Cohort 2.

PROCEDURES

This study will last twelve (12) months, with approximately six (6) months for each cohort. The participants in Cohort 2 need at least four visits to NIH. After your first visit, study visits will happen every month and as needed. The visits will last between four to six hours. The tests scheduled at each visit may be split and completed within seven days (including the seventh day) from the visit date.

While you are enrolled in this study, you may receive standard-of-care therapy at the NIH or your own doctors under this protocol. If you receive this therapy at NIH, you will sign separate consent forms for risks associated with any standard-of-care procedures, drugs or other treatments that are not described in this consent. You will stay under the care of your own doctors for your general medical care while you are in this study.

At your first visit, we will also ask you about your medical and eye disease history and perform an eye exam. The eye exam may be done through your participation in another NEI study. If your exam results indicate that you are able to be in this study, you will be given this consent so that you can decide if you want to participate.

If you are able to be in this study and agree to participate, we will perform initial examinations which will include a questionnaire. This questionnaire will ask you about problems that affect your eyes under different lighting conditions. You will be asked to complete this questionnaire at each visit.

If you want to participate and you are enrolled in Cohort 2, you will be given instructions on how to take three vitamin A pills by mouth twice a day for one month. You will need to record the time when you take your pills every day in a diary that we will give you. You will need to bring the diary and your pill bottle with any unused study pills to each visit.

At every visit, we will ask you about your health and what medications including any vitamins or supplements you are taking.

At each study visit, you will have some or all of the following tests.

Eye Examination: The eye examination includes testing how well you see, measuring your eye pressure, and checking your eye movements. For examination of the inside of the eye, your pupil will be dilated with eye drops. While your eyes are dilated, we will take pictures of the retina and the inside of your eye and will measure the thickness of your retina.

Blood Draw: Blood will be drawn through a needle in your arm. We will draw no more than 5 mL (one teaspoon) of blood at any one time. In most cases, blood will be drawn only once. The blood will be drawn to check your blood chemistry and how well your kidneys are functioning. If we are unable to use the first sample we collect, we will draw the blood again.

Dark Adaptation Protocol: This 20-40 minute procedure measures how fast your eyes recover when exposed to decreasing levels of light and how sensitive your eyes

are to these conditions. This procedure will be performed on your study eye while your pupil is dilated with eye drops.

The dark adaptometer is a metal box with a camera inside. You will be given a handheld device to push a button when you see a light in the machine. In this study, you will be seated at the machine in a dark room with your forehead and chin aligned in front of the box. To begin, we will give you a few practice runs for training (approximately two minutes). The real study begins with a bright flash of light.

After the bright flash of light, you will press the button as soon as you see the dim lights inside the box.

If you complete the dark adaptation protocol within 40 minutes, we would also like to perform the shortened procedure to compare with your first dark adaptation procedure. However, you do not have to have this test repeated if you do not want to. If you agree, we will ask you to wait 20 minutes before performing the shortened procedure.

Urine Tests: If you are able to get pregnant you will have a urine pregnancy test.

STORAGE AND SHARING OF SAMPLES AND DATA

Your data will be stored securely on the NIH campus. Your name and identifying information will not be on the data. The data will either have a code that links to your identifying information or will be stored without a code linking them to you. If they are coded, the key to the code will be kept at NIH in a separate, secure area and will not be shared.

Your data may be shared with others, including those not at NIH. Your data may be sent to a repository for storage. Your data may be used for other research projects, including those not related to RPD if you agree. Some repositories restrict access to the data they contain to researchers and projects they approve. Some repositories permit unrestricted access.

Research using data from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your data.

Please initial on the line below that reflects your choice:

_____YES My data may be used for other research projects including those not related to RPD.

_____NO I do not want my data used for other research projects.

If you withdraw from this research study before it is done, we will keep and continue to use samples and data that have already been collected. Your privacy will be protected as much as possible.

RISKS, INCONVENIENCES AND DISCOMFORTS

Risks of Eye Examination: There is minimal medical risk from the tests of vision, measuring eye pressure or retinal thickness or eye photography. The eye drops used to dilate your eyes may sting. You may have glare and blurry vision for several hours while your eyes are dilated. Some people are allergic to eye drops, while others experience a temporary increase in eye pressure. Your eye could become red or painful. A brief flash from eye photography equipment may cause temporary discomfort. There is a rare instance in which the cornea may be scratched during measurement, causing a painful scratch, but it heals quickly with no lasting effects. These problems will be treated if they occur.

Risks of Dark Adaptation Protocol: There is minimal medical risk from this procedure. They are the same as the risks of the eye examination. However, due to the need to focus during the entire testing period (20-40 minutes), there may be some discomfort or fatigue and you may be unable to complete the test due to loss of motivation or attention. If you are unable to complete the test, you will be withdrawn from the study.

If the dark adaptometer device times out during the testing period or the test cannot be completed correctly, returning to the clinic a week later to complete another dark adaptation procedure may be inconvenient.

Risks of Medical/Ophthalmic History: There is minimal medical risk associated with asking you about your medical and eye disease history.

Risks of Blood Drawing: You may have some discomfort and bruising from the needle insertion. Some people feel light-headed or faint.

Risks of Vitamin A Use: Vitamin A should be used with caution when combined with blood thinning medication, tetracycline antibiotics, and retinoid medications. It may decrease the effectiveness of a drug or supplement and may impair drug or supplement absorption.

Taking a high dose of vitamin A may cause toxicity (harm or danger). The potential toxic effects are different depending on the dose and length of time of supplementation. Acute (short term) may rarely include increased pressure in the head leading to vomiting or vision changes, or liver damage. Chronic (long term/several years of supplementation) can have adverse effects including

osteoporosis (pain in the joints or bones), anemia (tiredness or weakness), dry skin, dryness of mucous membranes (lining on surface of organs or body cavities), or hair loss.

If you are on Coumadin® (Warfarin) at time of enrollment, you must visit your prescribing physician to check your Coumadin® status within two-four weeks after initiating vitamin A to have your Coumadin® regimen adjusted if necessary (as taking vitamin A may require a decrease of your medication dose).

Risks of Storage and Sharing of Samples and Data: Even though we will remove information that could identify you from samples and data that are sent to repositories or shared, there is a very small chance that the samples and data could be identified as yours.

CAUTION: PARTICIPANTS WITH CHILDBEARING POTENTIAL OR WHO ARE ABLE TO FATHER A CHILD

There is a possible risk of deformity to a fetus if a participant of childbearing potential consumes high doses (i.e., greater than 25,000 IU/day) of vitamin A during pregnancy. No one should enter this study that plans on fathering a child or getting pregnant for the duration of the study. Participants must use at least one effective form of contraception while in this study and for one week after the last dose of vitamin A.

If you become pregnant (or get someone pregnant) while in this study, you must report the pregnancy immediately to a study doctor. We will arrange for a consultation with the NIH OB/Gyn service for evaluation and counseling and we will continue to follow the pregnancy even after you stop taking Vitamin A.

ANTICIPATED BENEFITS

You may benefit from participating in this study, if the vitamin A supplementation improves your vision. Your participation will help us learn more about RPD, dark adaptation and vitamin A that might help you or others in the future.

RIGHT OF WITHDRAWAL AND CONDITIONS FOR EARLY WITHDRAWAL

You may withdraw from the study at any time and for any reason without loss of benefits or privileges to which you are otherwise entitled. We can remove you from the study at any time if we believe that continuation is not in your best medical interest or if you are unable to comply with the requirements of the study.

DISCUSSION OF NEW FINDINGS WITH YOU

We will give you the results of all of your eye examinations. With your written request, we will send reports to your own doctors.

We will share with you in a timely manner any information we learn that may affect your willingness to continue to participate in the study. Data from the eye examinations and dark adaptometer including your status at baseline and any changes that have occurred will be shared with you at each visit.

Once all participants have completed the study, we will analyze the results and share them with you. Please let us know if you change your address or telephone number so that we can provide you this information.

ALTERNATIVES TO PARTICIPATION OR TREATMENT

You may choose not to participate in this study but to continue to receive standard care for RPD from your own physicians.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

This study will cover the costs of travel to and from the Clinical Center, lodging and meals. You will be reimbursed for these costs. If you require additional financial assistance, you may be able to receive supplemental reimbursement. Requests for supplemental reimbursement will be evaluated on a case-by-case basis for valid financial and/or medical need.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or

the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on 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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

When we store your data, we take precautions to protect your information from others that should not have access to it. When we share your data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your data.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Eye and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as

described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious

disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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, [redacted]. Other researchers you may call are: [redacted]. You may also call the NIH Clinical Center Patient Representative at [redacted], or the NIH Office of IRB Operations at [redacted], if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.