DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
Effects of Ketosis on CNS Oxygen Toxicity - II

Phase 1 Adult Consent Form

CONCISE SUMMARY

The purpose of this research study is to understand how ketogenic food products affect oxygen toxicity in undersea divers. We hope this will provide a starting point to develop methods for improving the safety of Navy divers, warfighters and submariners.

Participants in the study will undergo a physical exam and blood testing as part of the screening process. Eligible subjects will be asked to consume ketone food products. Blood samples will be collected every 30 to 60 minutes for up to 6 hours afterward.

The most common risks associated with study activities include drawing blood (momentary discomfort and/or bruising, infection, excess bleeding, clotting, or fainting) and pain associated with catheter placement. Risks associated with the ketogenic food products are nausea, vomiting, diarrhea, abdominal cramps and gas, mild intermittent constipation (difficulty moving your bowels) and mild intermittent hunger.

If you are interested in learning more about this study, please continue to read below.

You are being asked to take part in this research study because you are a healthy male or female between the age of 18 and 39 years of age.

Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As the study staff discusses this consent form with you please ask him or her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. Please tell the study staff if you are taking part in another research study.

If you are currently taking part in another research study, please tell the study staff at this time.

Dr. Bruce Derrick will conduct the study. It is funded by Naval Sea Systems Command. The sponsor of this study, Naval Sea Systems Command, will pay Duke University to perform this research, and these funds may reimburse part of Dr. Derrick's salary.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate Dr. Bruce Derrick will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

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WHY IS THIS STUDY BEING DONE?
The purpose of this study is to understand how ketogenic food products affects oxygen toxicity in undersea divers. Oxygen toxicity affecting the central nervous system, mainly the brain, is a result of breathing higher than normal oxygen levels at elevated pressures as can be seen in SCUBA diving or inside a hyperbaric (pressure) chamber. This is a condition that may cause a wide variety of symptoms such as: vision disturbances, ear-ringing, nausea, twitching, irritability, dizziness, and potentially loss of consciousness or seizure. Because ketone food products have been used to reduce or eliminate seizures in humans, it may be beneficial to reduce oxygen toxicity as well. We hope this study will provide a help to develop practical and useful methods for improving the safety of undersea Navy divers, warfighters and submariners.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 70 people will take part in this study at Duke.

WHAT IS INVOLVED IN THE STUDY?
Before you continue reading there are several important considerations:

- Study participation is voluntary.
- Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.
- You may discontinue the study at any point.
- Nonparticipation or withdrawal from this study will not affect your job status if you are a Duke employee and will not affect your grades if you are a Duke student.
- If you wish to participate in the next phase of this study you must wait at least one week after completing the study procedures below.

Pre-Study Procedures
If you agree to be in this study, you will be asked to sign and date this consent form. You will undergo the following tests and procedures to determine if you are eligible to participate in this study.

- You will initially participate in a subject briefing and have an opportunity to ask any questions regarding the study, particularly the expected discomforts and your right to stop participation at any time.
- You must pass a screening physical prior to the start of the study.
- You will have blood samples drawn to look at the biochemicals in your blood.
- You will have an electrocardiogram (EKG) performed looking at your heart's electrical activity.
- If you are a woman who could possibly become pregnant, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study.
- You may be tested for COVID-19 1-2 days prior to the experimental day. The experiment will be postponed if you test positive.

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Study procedures

- You will be asked not to eat after dinner time the night before the study, (7:30 pm).
- On the experimental day, you will be asked to come into the lab well hydrated at a designated time in the morning, but without eating breakfast or consuming any caffeine.
- Female subjects will have a urine pregnancy test
- Vital signs will be taken.
- You will have an intravenous catheter placed for collecting blood samples. Baseline blood samples will be drawn for clinical testing.
- You will be given a standardized breakfast followed by ketogenic food products to help boost your ketone levels and provide extra energy for the experiment. Participants will consume the ketone food products one, two or three times, 30 minutes apart, depending on your assigned study number.
    - The ketogenic food products are made up of three components. The first two are mixed together in water and consumed as a "shake": ketone salts, primarily beta-hydroxybutyrate, a ketone that is naturally occurring in the body, which will help raise your body's ketone levels prior to the experiment and provide energy. The second part of the shake is a "medium chain triglyceride" which is a form of fat that your body can use as fuel during exercise. You will only drink this shake only once.
    - The third food product is a "ketone diester" of beta-hydroxybutyrate and acetoacetate which are also naturally occurring in the body and also help raise your body's ketone levels. Because the ketone diester liquid does not taste good, the liquid has been placed in "gel-caps" so you can drink this like a pill without needing to taste the liquid. Each person will consume a number of gel-caps once, two or three times, 30 minutes apart for 60 minutes. The number of gel-caps will increase as the study goes on, and will depend on how participants tolerate the ketones. The food products are commercially available from vendors on-line or at stores.
- Blood samples will be taken from your catheter every 30 minutes for 3 hours and then every 60 minutes at hour 4, 5 and 6 after you have had the ketone food products. The maximum amount of blood drawn during any one experiment will be approximately 110 ml which is about 8 tablespoons. These blood samples will be evaluated for ketone levels.
- You will be monitored for side effects throughout the experiment.
- After collection of the last blood sample your catheter will be removed.
- A member of the study team will call you the evening after your experiment to ask about any side effects you may have.
- You will return to the laboratory within the following 1-3 days for collection of vital signs and a final blood sample.

HOW LONG WILL I BE IN THIS STUDY?
From the day of enrollment to the end of study will take approximately 2-3 weeks. The pre-study session described earlier will generally require 2-3 hours. Each test day will require approximately 7 hours.

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WHAT ARE THE RISKS OF THE STUDY?
Most Likely:

- Risks associated with drawing blood from your arm: These risks are momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.
- Pain associated with catheter placement: Placement of this catheter will be performed after injection of local anesthetic (numbing medicine) and is not normally associated with major discomfort, but pain can result.
- Risks associated with consuming the ketone food products: Nausea, vomiting, diarrhea, abdominal cramps, mild intermittent constipation (difficulty moving your bowels), and mild intermittent hunger were mentioned by subjects in other studies.

Less likely:

- Risks associated with catheter placement: Infection and allergic reaction to the local anesthetic. Other risks include damage to the vein that the catheter is being put through or clot formation in the vein which usually gets better in a few days.

Drug and Food Interactions
For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study.

Reproductive Risks
For women: Pregnancy affects how your body handles food, and could affect the study results. In addition, the effects of the ketogenic food products on a developing pregnancy are not known. If you could possibly become pregnant, pregnancy tests will be done at the pre-study visit and laboratory visit as described above. Although there is no risk to a pregnancy between the pre-study visit and laboratory visit, if you become pregnant between visits you will not be able to continue in the study. You should either abstain completely from vaginal intercourse during the study or use an effective method of birth control until the last study visit.

There may also be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
There will not be any direct benefits to you if you decide to participate in this research project. However, your participation with the project may help researchers to better understand how to use ketone food products to improve the safety of divers and military personnel.

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WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

All of these tests are being done only because you are in this study. As part of the study, Dr. Derrick and his study team will report the results of your study-related tests to the U.S. Navy. Study data which may include subject number, age, blood sample values, body measurements like height and weight be shared with Dr. Dominic D'Agostino at the University of South Florida for additional analysis. No other personally identifiable information such as your name or date of birth will be shared.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, the U.S. Navy, and/or the Duke University Health System Institutional Review Board. If your research records are reviewed by any of these groups, they may also need to review your entire medical record.

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research will be destroyed or information identifying you will be removed from the study results at DUHS.

This information may be further disclosed by the sponsor of this study, the U.S. Navy. If disclosed by the sponsor, the information is no longer covered by the federal privacy regulations. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by the federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

Subject's information and blood samples collected as part of the research, even if identifiers have been removed, will not be used or distributed for future research studies.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

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Photographs are taken to demonstrate protocols used in research studies. You will be asked if you agree to be photographed before any are taken. If taken, such photographs might be presented at meetings describing the research, in which case a bar will be placed in the photograph over the area of your eyes to make the photograph less identifiable. You will not be identified nor will your individual results discussed in such cases.

Please read the sentence below and put your subject initial next to your choice. You may participate in the study, without allowing your photograph to be taken.

_____ "Yes, I agree to be photographed."

_____ "No, I do not agree to be photographed."

All of the blood studies are being done only because you are in this study. The study results will not be given to you or sent to your physician unless, in the opinion of one of the study physicians, information important to your future health is learned.

WHAT ARE THE COSTS?
There are no costs to you for participating in this research project.

WHAT ABOUT COMPENSATION?
You will be compensated for participating in this study. You will receive $50 after completion of the initial screening visit. You will receive $300 for completion of the experimental trial.

The collection of your social security number by the Duke study team is required in order to set up payment. Payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual exceeds $600 in any one calendar year, Duke University is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of Duke University exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the IRS.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., your Duke physicians or the study sponsor, the Office of Naval Research, to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact Dr. Bruce Derrick at (919) 684-6726 during regular business hours and at his cell phone (315) 440-2565 or pager (919) 970-9792 after hours and on weekends and holidays.

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WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. You may withdraw your authorization for us to use your data that have already been collected (other than data needed to keep track of your withdrawal), but you must do this in writing. If you withdraw from the study, no new data about you will be collected for study purposes other than data needed to keep track of your withdrawal. All data that have already been collected for study purposes will be kept on file by the study doctor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. Nonparticipation or withdrawal from this study will not affect your job status if you are a Duke employee and will not affect your grades if you are a Duke student. If you do decide to withdraw, we ask that you contact Dr. Derrick in writing and let him know that you are withdrawing from the study. His mailing address is: DUMC Box 3823 Duke University Medical Center, Durham, NC 27710.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your study doctor may also decide to take you off this study if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. Reasons why this might occur include your inability to equalize the pressure in your middle ears during a hyperbaric chamber dive, a problem with a venous or arterial catheter or if the sponsor decides to discontinue the study.

Your samples and/or data may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your samples or data, we will no longer be able to identify and destroy them.

The use of your data and samples may result in commercial profit. You will not be compensated for the use of your data and samples other than what is described in this consent form.

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.

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WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns or suggestions about the research, contact Dr. Bruce Derrick at (919) 684-6726 during regular business hours and at his cell phone (315) 440-2565 or pager (919) 970-9792 after hours and on weekends and holidays.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time