Duke University Health System

Consent To Participate in Research Study

IRB# Pro00107090

Diaphragm Function and Diver Endurance

NCT04679402

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"Diaphragm Function and Diver Endurance" IRB #Pro00107090

Concise Summary

The purposes of this study are to: (1) test a method that could increase personal endurance and reduce excessive rise in blood carbon dioxide during underwater exercise in divers; and (2) understand the mechanisms by which red blood cells transport oxygen and carbon dioxide and the degree to which this affects exercise capacity.

Stamina during a dive and the ability to control blood carbon dioxide depend on the function of the respiratory muscles (mainly diaphragm). It has been shown that training the breathing muscles can increase exercise endurance, including during a dive. Previous studies from our lab have demonstrated that muscle training can be enhanced by simultaneous breathing of a low, non-toxic (200 ppm) level of carbon monoxide.

In this study, we will test the effect of daily respiratory muscle training with and without added carbon monoxide on breathing muscle performance and underwater exercise endurance during a dive to 55 feet of sea water, while measuring blood carbon dioxide and lactic acid levels obtained from a small catheter placed in a wrist artery. The study will require some preliminary testing for eligibility, followed by the dive, then one month of daily 30-minute breathing exercises. Following that, a second diving endurance test will occur.

Red blood cells obtained during the study will be sent to another lab where their ability to transport oxygen and carbon dioxide will be tested. The risks will include: (1) insertion of a small tube into an artery in your wrist, which could cause bruising and also blockage of the blood supply that could lead to permanent injury or loss of your thumb or hand; (2) adverse effects of chamber compression on your ears or sinuses, leading to pain and hearing loss; (3) decompression sickness due to gas bubbles forming in tissues and blood, which can cause pain in the joints, skin rash, numbness, damage to the brain, spinal cord, or lung leading to disability, and even death. Benefits may include learning a method of increasing your exercise endurance.

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 45 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 your study doctor or study staff discuss 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.

A grant from the US Navy will sponsor this study. Portions of Dr. Moon's and his research team's salaries will be paid by this grant.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Drs. Richard Moon, Bruce Derrick and Melanie Hollidge will conduct the study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine whether training of the respiratory muscles with added low-dose non-toxic levels of carbon monoxide will improve underwater endurance. A secondary aim is to assess red blood cells

and determine their ability to transport oxygen and carbon dioxide, and assess whether this may also affect endurance during an underwater dive.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 60 people will participate in this study.

WHAT IS INVOLVED IN THE STUDY?
If you agree to be in this study, you will be asked to sign and date this consent form. You will have the following tests and procedures to make sure that you are eligible:

Pre-Study Procedures

A. 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.

B. In order to participate in this study you must be 18-45 years of age, a non-smoker, not pregnant, not have either sickle cell disease or sickle cell trait and pass a screening physical prior to the start of the test activities in the study. You will complete a medical history and a physical exam.

C. You will undergo a 12-lead electrocardiogram (ECG: a painless test that measures the electrical action of your heart), and blow into a machine to determine the fitness of your lungs (spirometry and maximum breathing capacity). Spirometry measures how much air you breathe in and breathe out, and how quickly you breathe out; maximum breathing capacity (MBC) measures how much air you can breathe in and out of the machine for 12 to 15 seconds. Your sensitivity to carbon dioxide will also be tested. This consists of breathing increasing levels of carbon dioxide and measuring the resulting increase in breathing (ventilatory sensitivity to carbon dioxide or so-called 'hypercapnic ventilatory response'). Each of these tests will require around 10 minutes.

D. If you are a woman who could get pregnant, you will provide a blood or urine sample for a pregnancy test before each dive.

E. If you are of African American descent, you will have blood drawn for screening of the sickle cell trait. Some information suggests that individuals with sickle cell trait may be at higher risk of sudden death during exercise. Whether this is the case for diving is not known with certainty, however this test is being performed out of caution and concern for the safety of our research participants.

F. You will perform a strenuous exercise test (VO_2max test) on a stationary bicycle over a 10-20 minute period at an increasing workload until you stop the exercise due to fatigue or discomfort. A doctor will monitor your heart rate and waveform (ECG) during this period. You will be unable to participate if your oxygen consumption at maximal effort is less than 35 mL/(kg*min) for males or less than 30 mL/(kg*min) for females (this intensity represents approximately 10 times the metabolic effort maintained at rest).

Investigational Research Study Activities
After the screening procedures described above you will perform the following on a separate day. Before these tests you will have only clear liquids for breakfast.

(1). Painless measurement of the thickness of your diaphragm using ultrasound. A mark will be placed on the ultrasound probe placement site using a long-lasting but temporary marker.

(2). Measurement of the maximum pressure exerted by your diaphragm during contraction against a pressure measuring device. This will be done by measuring by passing a small tube (nasogastric tube) through your nose into your stomach. In order to minimize any discomfort a small amount of gel containing a local anesthetic ('numbing medicine') will first be applied to the inside of your nose.

(3). Voluntary breathing endurance test. This consists of a measurement of how long you can breathe at maximum effort against a resistance, typically a few minutes.

(4). VO_2max test on a stationary bicycle while underwater.

Following this, on the same day or a separate day, you will perform the following:

Underwater endurance test. Prior to this test a catheter will be inserted into an artery in your wrist after injection of local anesthetic. You will then enter the hyperbaric chamber, which will be compressed to an equivalent depth of 55 feet and exercise underwater at a level equal to between 70% and 85% of your previously measured peak work capacity until you cannot continue. Blood samples will be obtained periodically to measure levels of oxygen, carbon dioxide, lactic acid and pyruvic acid.

This will then be followed by respiratory muscle training. This will consist of 4 weeks of daily, 5 days per week 30-minute sessions, during which you will breathe through a mouthpiece with a nose clip. Every 30 seconds a beep will signal you to take a full inhalation and exhalation, which will occur against a resistance. The resistance will be increased by a small amount each week. You will be randomly assigned (like the flip of a coin) to breathe either air or a low concentration of carbon monoxide during these training sessions. During the final week, at the end of one of these sessions, a teaspoonful of blood will be obtained to measure carbon monoxide level in the blood. If you are selected to breathe carbon monoxide, the concentration will be 200 parts per million, a non-toxic level. This concentration of carbon monoxide has previously been safely breathed during studies in our lab.

You will then undergo ventilatory sensitivity to carbon dioxide testing, voluntary breathing endurance test, diaphragm thickness measurement, maximum diaphragm pressure measurement, spirometry, MVV and a final underwater endurance test as described above.

THERE ARE SEVERAL IMPORTANT CONSIDERATIONS:

- Participation in this study is voluntary.
- You may terminate your participation at any time.
- 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.

HOW LONG WILL I BE IN THIS STUDY?

The pre-study sessions described earlier will generally require 4-5 hours on one day. In order to maximize each subject's performance on the underwater exercise apparatus, familiarization will be required, and may require some additional time on an individual basis (between 1 and 5 hours). The main research activities will take place at least one day later. The first dive will occur on a third day, requiring around 3 hours total time. This will then be followed by daily respiratory muscle exercise training, each session lasting around 30 minutes. The final day of testing and the second dive will require 4-5 hours.

WHAT ARE THE RISKS AND DISCOMFORTS OF THE STUDY?

As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose:

More likely:

1. Risks associated with drawing blood from your arm: These include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.
2. Injection of local anesthetic prior to placement of the arterial catheter: Pain can occur, although this is usually short-lived.
3. Barotrauma: With compression there is occasional difficulty getting the air pressure in the ears, sinuses, teeth, lungs and intestines to equal the increasing pressure outside the body. Such problems may cause pain and the production of fluid in these spaces. Other possible effects include hearing loss, inflammation of the ear and sinusitis. Usually, these problems are temporary and clear in a few days. Very rarely permanent problems occur. If any discomfort is felt during compression, the personnel in the laboratory should be immediately notified so that corrective measures can be taken.
4. Discomfort or nosebleed from placement of the nasogastric tube in your stomach.

Less likely:

1. Risks of decompression sickness (DCS): You may develop signs or symptoms of DCS as a result of the dive. DCS symptoms are due to gas bubbles forming in tissues and blood. The most common symptoms are usually joint "awareness," pain in the joints (mostly mild pain in the knees or ankles and occasionally elbows or shoulders), skin rash, and numbness. Other possible symptoms include coughing or chest pain on breathing (the chokes), blurred vision, vertigo, hearing loss, tingling, numbness, weakness, inappropriate fatigue, and severe headache. This can involve damage to the brain, spinal cord, or lung leading to disability, and even death. The risk of serious decompression sickness in the test is very low. We will monitor you for the presence of bubbles in the veins and arteries using ultrasound. You will be removed from an experiment if arterial bubbles are found even if no symptoms of decompression sickness develop.

   Treatment of DCS: Recompression in a hyperbaric chamber is usually effective for treatment of DCS. Recompression therapy is available on site in the Duke Center for Hyperbaric Medicine and Environmental Physiology where the altitude studies will take place. Recompression therapy is very effective in treating decompression sickness especially if it is administered quickly after symptom onset. Nevertheless, there is a very small risk of a serious episode of decompression sickness that will not completely resolve with recompression treatment.

   You will be monitored constantly during the research study activities, and there will be medical staff available at all times who are prepared to intervene if there any problems.

2. Risks associated with equipment failure: If there is mechanical or electrical failure of part of the pressure tank or of the equipment which keeps it operating safely, the exposed humans could be seriously injured or even killed. If a fire occurs within the pressure tank, all exposed humans could get burned or asphyxiated (suffocated). However, the Duke hyperbaric chambers have a very good safety record: in over 50 years of operation, there have been no instances of serious structural failure, and no resulting injuries to personnel or

experimental subjects. Nonetheless, the possibility of equipment failure, however remote, cannot be completely eliminated. Minor problems have happened including:

- A structural problem that occurred during an altitude study. In this problem the O-ring seal on the chamber's "medical lock" door was damaged during an altitude study when a subject improperly closed the door. The chamber lost vacuum and the simulated altitude decreased from 11,500 to 8,000 causing some brief discomfort due to ear popping in the subjects before it was recognized and corrected. A procedural checklist to minimize the risk of similar future events was put into place. This could not occur during a dive, as planned for this study.
- A fire occurred during compression of an unoccupied chamber due to the use of a ball valve containing a flammable substance (nylon) through which 100% oxygen was being delivered at high pressure. This occurred in 1980, since which time all new equipment is subjected to evaluation and testing before its use.

3. Risks associated with a maximal exercise test: The bicycle test you may be asked to perform is a graded VO_2 peak test (it measures your use of oxygen during exercise). What this means is that the workload will gradually be increased on the bike, and the test continues until you are exhausted, or the attending physician stops the test based on information he or she gathers about you during the test. The physician has well-defined rules to end the exercise, but the normal reason to stop the test in a healthy person is exhaustion. This may not be a pleasant end-point for the test, especially if you rarely exercise to exhaustion. Occasionally, people who exercise feel lightheaded, become short of breath, develop chest pain, or develop irregularities of their heart beat that are natural responses. During recovery from exercise, some may become faint. On very rare occasions death (0.005% or 1 in 20,000) or heart attack (0.02% or 1 in 5,000) has occurred during exercise. These risks are associated with exercise testing that has been documented primarily from a high-risk population (patients with heart disease or suspected heart disease). The likelihood of these problems occurring in asymptomatic (neither causing nor displaying symptoms), healthy subjects is low, but not impossible. The attending technician will explain the bicycle exercise to you in great detail. An Advanced Cardiac Life Support (ACLS)-certified physician and two test operators certified in cardiopulmonary resuscitation (CPR) will be present during the exercise testing and ECG monitoring will be used as a safety precaution.
4. Risks associated with catheter placement: Infection and allergic reaction to the local anesthetic. Arterial catheter insertion in the wrist can cause bruising and also blockage of the blood supply that could lead to permanent injury or loss of your thumb or hand.
5. Perforation of the soft tissues of your throat or esophagus during placement of the nasogastric tube: If this were to happen it could lead to chest infection or lung collapse requiring surgery.
6. Risks to an unborn child:

   Female. Pregnancy can affect your body's exercise capacity. In addition, low levels of oxygen or exposure to carbon monoxide can have harmful effects for a developing pregnancy, especially later in pregnancy. Women who are pregnant, planning a pregnancy, or breastfeeding are not allowed to participate in this study.

   The effects of diving or carbon monoxide exposure in very early pregnancy are not known. If you are a woman who could possibly become pregnant, a blood or urine pregnancy test will be done before each dive session. Because pregnancy tests do not give positive results in the week after conception, it is possible to miss a very

early pregnancy. If you are sexually active with a partner who is able to father children, you should either abstain completely from vaginal intercourse from the time of your screening visit until after the last study session, or use an effective method of birth control for the same length of time. Your study doctor will discuss appropriate methods of birth control with you.

If you think there's any chance you might be pregnant during the study, let your study physician know right away.

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

Risks of Drawing Blood: A small blood sample (approximately 2 teaspoons) will be obtained, processed and DNA extracted and stored in the Duke Biobank. Blood will also be sent to Case Western Reserve University for analysis, but will not contain any identifiers.

Genome Wide Association Studies (GWAS):

As part of this study a genome-wide association study (GWAS) will be performed. GWAS studies look at the genetic differences between individuals that may be found in the human genome (the complete set of all human genes) to find out if there is a relationship between certain genes and the efficiency with which their red blood cells transport oxygen and carbon dioxide. Samples will also be stored in the Duke Biobank repository (a repository is a place where data are stored for use in future research). The data will not be labeled with any information that can be used to identify you.

Participation in genetic studies: The genetic studies described are for research purposes only. Therefore, you will receive no results from this study (except as described below). It is not the purpose of this study to look for or provide you with any medical information or diagnoses relating to your present condition or any other disease or illness. The research tests are not being used as diagnostic tests for any disease or illness. Your participation in this study is not a substitute for your regular medical care or check-ups.

Research Results: Through this research, we may find that you have an abnormal gene which indicates a risk for developing a disease at some time in the future. It is also possible that the research results may indirectly provide unexpected personal information about you or your family (such as ethnic/racial background or an unknown genetic relationship between family members). Please talk with the study doctor if you have any questions or concerns about the genetic testing being done in this research study. He/she may also refer you to a genetic counselor for further information.

Incidental Findings: It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician unless the information indicates that you may be at risk for a serious illness known at the time of testing to be treatable. In that case, we will attempt to notify you using the contact information you have provided, so that you can speak with Dr. Moon at Duke University Health System (DUHS). DUHS staff will not provide this information in a voice mail, email, or otherwise prior to contacting you. Please notify us of any change in your contact information.

If you do not want to be notified of any incidental findings, please initial below.

_____ Please do not notify me of any incidental findings obtained from this research.

If you prefer, we can ask you at the time of notification whether or not you want to receive incidental findings information. In this case, please initial below.

_____ Please ask me at the time of notification whether or not I want to receive incidental findings information.

If at any time during or after the study you change your mind about whether or not you would like to be notified, you can contact us at 919-684-8762.

After providing the information to you, Dr. Moon may arrange for you to meet with him and/or a genetic counselor or refer you to another appropriate health care provider to review the incidental findings information with you or your physician.

Use and ownership of samples: By agreeing to participate in this research, you authorize DUHS and members of its staff to use your tissue, blood or other samples for the purposes described in this consent form. DUHS will maintain these samples indefinitely or until they are exhausted.

These samples will not be available to you for diagnostic or therapeutic purposes. Therefore, for any future diagnostic testing or treatments, a new sample will be obtained from you. Blood collected as part of this study may be valuable for scientific, research, or teaching purposes or for the development of a new medical or commercial product. DUHS and/or the developers will assert all rights of ownership in the samples and all rights arising from use of the samples. There is no plan to compensate you for any use of the samples.

Availability/withdrawal of samples: You will not have access to the sample once it is obtained. Samples may be stored indefinitely. If you decide to withdraw your permission to use your samples in this research project, please contact the study doctor, Dr. Richard Moon, in writing and let him know you are withdrawing your permission for your samples to be stored and used for this or future research. His mailing address is Dept. of Anesthesiology, Box 3094, Duke University Medical Center, Durham, NC 27710. At that time, we will ask you to indicate in writing if you want your unused samples destroyed or if your samples (with all identifying information removed that would link the sample to you) could be used in research. Data collected using your sample before your withdrawal will continue to be used as part of the study.

Potential Risks and the Genetic Information Non-Discrimination Act (GINA): There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential information, but this cannot be guaranteed. The genetic information obtained as a result of your participation in this research will not be included in your medical record. Information from which you may be personally identified will be maintained in a confidential, secure location at DUHS, accessible only by authorized members of the study team, and will not be disclosed to third parties except as described in this consent form, with your permission, or as may be required by law.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

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. Study records that identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of Duke University Health System (DUHS). For records disclosed outside of DUHS, you will be assigned a unique code number. The key to the code will be kept in a locked file in the Duke Hyperbaric Center, Room 0587A.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration 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. As part of the study, results of your study-related laboratory tests, x-rays, and procedures may be reported to the Navy. A representative from the Navy may be present at certain study visits/procedures. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives and affiliates of the US Navy, the Duke University Health System Institutional Review Board, and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record. 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.

All of the blood and x-ray studies are being done only because you are in this study. The study results will be provided to you but will not be sent to your physician unless you request it.

Expiration date or event for the retention of records: The study results will be retained in your research record forever. Any research information in your medical record will also be kept indefinitely.

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.

PHYSICIAN AVAILABILITY

A doctor experienced with altitude and hyperbaric medicine is available before, during, and after the test. This includes the initial medical screening and a pre-test physical to ensure that you are healthy before the test. During the test, the physician will be available to follow your progress. In the event of a problem, the doctor will stop the test and will direct any treatment you need, including recompression in the hyperbaric chamber, and medical

follow-up after a treatment. You will have access to the doctor to specifically address any post-test concerns at any time during or following the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

A benefit to you being in the study is the possibility to observe the effect that respiratory muscle training may have on your endurance during steady exercise. This study may also provide a safe method to maximize underwater performance of Navy divers.

ARE THERE ANY RESTRICTIONS ON MY ACTIVITIES BEFORE OR AFTER THE STUDY?

You will be required to be available in person or by phone for 24 hours after completion of the study to be checked for symptoms of DCS. If you do develop symptoms you must be available and willing to come to Duke Hospital for evaluation in person. You must not fly in an airplane for 24 hours after completion of the study.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?

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. No matter what you decide to do, your decision will not affect your care.

1. "I agree to be photographed."

_____
Subject's Initials

2. "I do not agree to be photographed."

_____
Subject's Initials

WHAT ARE THE COSTS?

There are no costs associated with participation in this study. If you require treatment for decompression sickness you will not be charged for the medical care.

WHAT ABOUT COMPENSATION?

You will receive $50 compensation only if you are accepted into the study but disqualified prior to the investigational activities because you do not successfully pass the medical evaluation, meet body composition requirements or exercise requirements. Total possible compensation for completion of the study is as follows:

Screen, including exercise tests	$50		
Underwater endurance test #1	$400		
Training Sessions			
#1	$10	**#11**	$20
#2	$11	**#12**	$21
#3	$12	**#13**	$22
#4	$13	**#14**	$23
#5	$14	**#15**	$24
#6	$15	**#16**	$27
#7	$16	**#17**	$28
#8	$17	**#18**	$29
#9	$18	**#19**	$30
#10	$19	**#20**	$31
Underwater endurance test #2	$400		
TOTAL POSSIBLE COMPENSATION	**$1,250**		

Payment received as compensation for participation in research is considered taxable income to the research participant. Research participant payments to a non-employee of Duke University adding up to $600 or more during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the Internal Revenue Service (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., or your Duke physicians 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. Moon at 919-684-8762 during regular business hours and at 919-970-5290 (pager) after hours and on weekends and holidays.

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

It is necessary that you read and understand several general principles that apply to everyone who takes part in this study:

1. Taking part in this study is entirely voluntary. 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. All data that have

already been collected for study purposes, and any new information about an adverse event related to the study, will be provided to the Duke University Health System.

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. If you do decide to withdraw, we ask that you contact Dr. Richard Moon in writing and let him know that you are withdrawing from the study. His mailing address is: PO Box 3094, Duke University Medical Center, Durham, NC 27710. At that time we will ask your permission to continue using all information about you that has already been collected as part of the study prior to your withdrawal.

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.

2. There will be no charge to you for taking part in this study.
3. Medical records are maintained according to hospital requirements. However, it should be noted that representatives of the Duke Institutional Review Board are eligible to review research records as a part of their responsibility to protect human subjects in research. Thus, complete confidentiality cannot be guaranteed.
4. We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

STORAGE OF SAMPLES

As part of this study, with your permission we would like to store and use your identifiable blood/urine/DNA samples for future research. If you agree to allow your blood/urine/DNA to be kept for future research with identifying information that could link your sample to you, you are free to change your mind at any time. Please read the sentence below and put your initials next to your choice. No matter what you decide to do, your decision will not affect your care.

"I **agree** to allow my identifiable blood/urine/DNA samples to be stored for future research"

_____

Subject's Initials

"I **do not agree** to allow my identifiable blood/urine/DNA samples to be stored for future research"

_____

Subject's Initials

If you opt-in and later decide that you do not want your blood/urine/DNA samples to be stored for future research, we ask that you contact Dr. Moon in writing and let him know you are withdrawing your permission for

your identifiable blood/urine/DNA to be used for future research. His mailing address is: **Dept. of Anesthesiology, Box 3094, Duke University Medical Center, Durham, NC 27710, USA**. At that we will ask you to indicate in writing if you want the unused identifiable blood/urine/DNA samples destroyed or if your samples (having all identifying information removed that would link the sample to you) could be used for other research.

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

A description of this clinical trial will be available on https://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.

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, questions or suggestions about the research, please contact the principal investigator (study doctor), Dr. Richard Moon (pager 919-970-5290), or co-investigators Dr. Bruce Derrick (pager 919-970-9792) or Dr. Melanie Hollidge (pager 919-970-0327). You will be given current contact phone and pager numbers for the 'on call' physician during the medical watch period following chamber exposures. These will be recorded on a disposable hospital wristband for you to wear for 48 hours following exposure in the hyperbaric chamber. For questions about your rights as a research participant, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

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