APPROVED
Expiration Date: N/A
2023-068-HYBL

**Institutional Review Board (IRB) for the Protection of Human Subjects**

**Date:** 01/03/2023

**IRB PROTOCOL NO.:** 2023-068
**Protocol Title:** Effect of skin rewarming after exercise cold stress upon LBNP tolerance
**Principal Investigator:** James Pearson, Ph.D.
**Faculty Advisor if Applicable:**
**Application:** New Submission
**Type of Review:** Expedited 3
Expedited 4

**Risk Level:** Minimal
**Renewal Review Level (If changed from original approval) if Applicable:**
**This Protocol involves a Vulnerable Population:**
**Expires:** N/A
**Externally funded:** **OSP #:** **Sponsor:**

Thank you for submitting your Request for IRB Review. The protocol identified above has been reviewed according to the policies of this institution and the provisions of applicable federal regulations. The review category is noted above, along with the expiration date, if applicable. In addition, the protocol may match more than one review category not listed.

Once human participant research has been approved, it is the Principal Investigator's (PI) responsibility to abide by the following:

- The PI must submit all protocol, recruitment, advertising, and consent form amendments/revisions to the IRB for approval.
  - The IRB must approve these changes prior to implementation.
- Changes in funding status must be reported to the IRB as quickly as possible to ensure funding requirements are met.
- The PI must promptly inform the IRB of all unanticipated serious adverse events (within 24 hours). All unanticipated adverse events must be reported to the IRB within 1 week (see 45CFR46.108(a)(4)(i)). Failure to comply with these federally mandated responsibilities may result in suspension or termination of the project. This includes possible exposure of research personnel or participants to COVID-19.
- The PI must submit a Continuing Review/Renewal appliciaton to the IRB at least ***10 business days prior to expiration***. For studies with no expiration, a brief check-in application is required annually.
- If you are a student, note that it is required to include the IRB approval letter to the library when you submit the dissertation/thesis.
- Notify the IRB when the study is complete.
- For in-person research, must halt research at anytime if notified to do so by the IRB due to changing COVID-19 related conditions or changes in campus, county, or state policy.

If you have any questions, please contact the Research Compliance Program Director in the Office of Sponsored Programs and Research Integrity at 719-255-3903 or irb@uccs.edu

Thank you for your concern about human subject protection issues, and good luck with your research.

Sincerely yours,

Zek Valkyrie, Ph.D.
IRB Reviewer

**University of Colorado**
**Colorado Springs (UCCS)**
**Consent to be a Research Subject**

**Title**: Effect of skin rewarming after exercise cold stress upon LBNP tolerance

**Principal Investigator**: James Pearson, PhD

**Funding Source**: none

**Key Information**

*Your consent to participate in this study is being requested and participation is voluntary. If you choose to give your consent to participate in this study, you are free to withdraw from the study at any time. The purpose of this research is to better understand how your tolerance to a lower body negative pressure test is affected in cold conditions. It is reasonable to expect that you will feel cold during some of the study visits and that you will experience physical exertion, increased breathing rate and sweating as a result of exercise. It is also reasonable to expect that you may experience nausea, light-headedness and/or nausea at the end of the lower body negative pressure test. Given that we are currenlty in the midst of the COVID-19 pandemic there may be an increased risk of infection to you in participating in this study given that you will spend time in a research laboratory with other research investigators whilst exercising. You may benefit from participating in this study due to an increased understanding of how your body functions during exercise and cold stress. This study will also help us understand whether the control of blood pressure and heart rate during a simulated hemorrhagic insult is different if you are cold relative to if you have a normal body temperature and identify if warming up your skin during thelower body negative pressure is helpful. The findings of this study may be of benefit to soldiers, firefighters, construction workers and police offers, all of whom are at increased risk of experiencing injury and blood loss as part of their profession, occassionally in cold enviuronments.*

Given that we are currently in the midst of the COVID-19 pandemic there may be an increased risk of infection to you in participating in this study given that you will spend time in a research laboratory with other research investigators whilst exercising. To mitigate the risk of exposure to COVID-19, the facemask or mouthpiece with nose clip ensemble will be fitted with a microbial filter. Where possible, we will also instruct you to instrument yourself to minimize contact with study investigators, such as when placing the facemask or mouthpiece with nose clip. Thorough disinfection procedure will be employed prior to each study visit. That is, all hard surfaces will be sanitized while facemask or mouthpiece with nose clip ensembles will all be thoroughly cleaned and sterilized with a solution called CIDEX to ensure that the risk of exposure to COVID-19 is minimized. Investigators will wear medical gloves throughout.

**Introduction**

You are being asked to be in a research study. This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. A member of the research team will describe this study to you and answer any questions. **It is entirely your choice. If you decide to take part, you can change your mind at any time and withdraw from the research study.**

Before making your decision:

- Please carefully read this form or have it read to you.
- Please ask questions about anything that is not clear.
-

Additionally, there are some exclusion criteria. If any of the following apply, then you may not be permitted to participate in this study at this time for your own safety:

- If you are taking any prescribed or over the counter medications that are known to affect the heart or blood vessels.
- If you have been diagnosed with major illness or disease.
- If you have a resting blood pressure above 150/80mmHg while seated.
- If you have previously had abdominal surgery.
- If you believe that you may be pregnant.
- If you are currently dehydrated, as assessed by urine sample.
- If you have ingested a caffeinated beverage such as coffee, tea, or an energy drink on the day of either study visits.
- If you are scheduled for an MRI within 7 days of taking the telemetric pill.

Feel free to take your time thinking about whether you would like to participate. By signing this form, you will not give up any legal rights.

**Study Overview** The purpose of this study is to investigate whether the control of the cardiovascular system during simulated blood loss (lower body negative pressure; LBNP) is different following rest or exercise in a cold environment and further, what is the influence of skin surface warming. We expect that in cold environments the tolerance to blood loss will improve and that skin surface warming will change the control of your heart and blood vessels.

**Procedures** You are being asked to be in this research study because you are a healthy person between the ages of 18-40, are not currently taking any prescribed or over the counter medications or nutritional supplements known to influence the heart or blood vessels, have not been diagnosed with any cardiovascular diseases, are not pregnant, and do not use tobacco/nicotine products. If you agree to be a research subject you will be scheduled for up to six study visits (Visits A B C D E and F) in a research laboratory (HYBL 302, 311, 313 or 338) or temperature-controlled room in the Hybl Center on the UCCS campus. All visits are voluntary. Visit A will last for approximately one hour. Visits B through F will last three to four hours each.

Procedures *Visit A: Maximal Exercise Test*
*This will be the first visit. In this visit you will wear a heart rate monitor, face mask or mouthpiece with a nose clip which will have a tube connected to a computer analysis system. The tube will collect the air you breathe out and analyze it. You will complete a maximal exercise test to exhaustion on a bike. Initially the test will start slowly requiring you to exercise at a very light intensity. The intensity will gradually increase until you reach a point where you are either no longer able to continue exercise or the investigator determines that the test is over (whichever comes first). This test will last approximately 20-25 minutes.*

*Visit B: Exercise in the cold followed by Lower body negative pressure whilst keeping the skin cold.*
*In this visit you will perform high intensity interval exercise on a cycle. The intensity of this exercise will vary from 90% of your maximal capacity for 60 seconds to 15% of your maximal effort for 90 seconds. You will perform approximately 15 of these intervals or you can stop exercise at any time if you are exhausted and can no longer continue to complete the intervals. You will complete this exercise in a cold room. Even in the cold room exercise may result in your internal body temperature increasing, so you may feel hot. You will be fitted with either the face mask or mouth piece and heart rate monitor as per visit A. During exercise you will also wear a tube lined suit. Once you have completed exercise you will transition from the exercise bike onto a medical bed where you will lay supine with the lower half of your body sealed inside a lower body negative pressure box. You will then undergo the lower body negative pressure test. The lower body negative pressure test causes fluid in your body to shift from your chest and upper body to your lower body. Suction will be applied inside the box to your lower body. The suction to your hips and legs will increase until you request to stop or*

*the researchers determine that the test is over (whichever comes first). This test can last between 5-25 minutes. During this lower body negative pressure test your skin will be kept cold.*

*Visit C: Exercise in the cold followed by Lower body negative pressure whilst returning the skin to normal temperature.*
*In this visit you will repeat the procedures outlined in Visit B above. However, during the lower body negative pressure test your skin will be rewarmed slightly so it returns to normal levels.*

*Visit D: Exercise in the cold followed by Lower body negative pressure whilst mildly heating the skin to feel warm.*
*In this visit you will repeat the procedures outlined in Visit B above. However, during this lower body negative pressure test your skin will be slightly heated.*

*Visit E: Exercise in the cold followed by Lower body negative pressure whilst heating the skin to feel hot.*
*In this visit you will repeat the procedures outlined in Visit B above. However, during this lower body negative pressure test your skin will be heated so that it feels hot.*

*Visit F: Exercise in a normal temperature followed by Lower body negative pressure.*
*In this visit you will perform high intensity interval exercise on a bike. The intensity of this exercise will vary from 90% of your maximal capacity for 60 seconds to 15% of your maximal effort for 90 seconds. You will perform approximately 15 of these intervals or you can stop exercise at any time if you are exhausted and can no longer continue to complete the intervals. You will complete this exercise in a normal temperature room. Even in the normal temperature room exercise may result in your internal body temperature increasing, so you may feel hot. You will be fitted with either the face mask or mouth piece and heart rate monitor as per visit A. During exercise you will also wear a tube lined suit. Once you have completed exercise you will transition from the exercise bike onto a medical bed where you will lay supine with the lower half of your body sealed inside a lower body negative pressure box. You will then undergo the lower body negative pressure test. The lower body negative pressure test causes fluid in your body to shift from your chest and upper body to your lower body. Suction will be applied inside the box to your lower body. The suction to your hips and legs will increase until you request to stop or the researchers determine that the test is over (whichever comes first). This test can last between 5-25 minutes. During this lower body negative pressure test your skin will be kept at a normal temperature.*

*During visits B, C, D, E and F we will place instrumentation on your body to measure:*

- *Brain blood flow using a transcranial Doppler machine. This will involve you wearing a headband used to hold two sensors at the side of your head that measure blood flow in your brain.*
- *Expired air from your mouth and nostrils using a face mask or mouthpiece with nose clip that is connected via plastic tubing to an analyzer.*
- *Large artery stiffness using a pressure sensor placed on the pulse in your neck, at the top of your leg and at your wrist. A wrist band will be used to hold the pressure sensor in place.*
- *Blood flow through the skin using two sensors called laser Doppler flowmeters. These will be combined with two discs the size of a quarter dollar, which will be used to attach the two sensors to your forearm.*

*At the end of each visit the quarter dollar sized discs will heat up a little and feel hot in a very small area for 30 minutes.*

- *Blood flow through your neck, leg, and upper arm using an ultrasound machine. The researchers will us a handheld sensor which will be temporarily placed on top of a blood vessel. These procedures are similar to those used to view babies in wombs of pregnant women.*
- *Blood pressure using a cuff wrapped around your finger, and upper arm.*
- *Heart rate by placing sticky sensors on your chest.*
- *Skin temperature by placing temperature sensors with adhesive tape on your forehead, hand, chest, back, arms and legs.*
- *Internal body temperature by asking you to self-insert a sterile rectal probe/thermocouple 10 cm past the anal sphincter. Alternatively, this measurement may be made by swallowing a sterile sensor with water.*
- *Tissue oxygenation of the thigh, calf, and/or deltoid muscle (quadriceps) by placing a non-invasive sensor on top of the skin of the thigh which will be surrounded by bandages to hold the sensors in place.*

*We will also ask you to provide a very small urine sample prior to the start of each study visit. The purpose of this is to ensure that you are properly hydrated. Finally, we will also take some skinfold measurements of the thigh, calf, and/or deltoid using calipers in order to help us interpret tissue oxygenation data.*

**Other people in this study**: Up to 100 people will participate in this study.

Risks and Discomforts It is likely that you will experience at least some level of discomfort owing to decreases in body temperature and the exertion of exercise. You will be informed exactly as to when temperatures will decrease and be continuously monitored for your own safety. However if you feel that the level of discomfort is too much please let one of the investigators know immediately and they will work to fix the problem. The potential risks and discomforts that are associated with all of the procedures are very small and detailed below.

All procedures: A normal and healthy blood pressure could be broadly considered to be 120/80mmHg, and this will both fluctuate considerably throughout the day and will be dependent on what you are doing. It is entirely normal for your blood pressure to temporarily slightly increase and decrease during all of the procedures in this study. Therefore, there is a very small risk that you may experience excessive increases or decreases in your blood pressure. We will monitor your blood pressure continuously in all these procedures and if your blood pressure increases by >75/50mmHg from your resting value or decreases to an absolute value below 80/50mmHg then we will stop the procedures immediately.

Exercise: During Visit A you will perform a maximal exercise test. It is likely that you will feel very tired at the end of this test as it requires you to exercise until you feel like you are out of breath. During visits B through F, you will perform high intensity interval exercise. This is where the exercise is hard for 60 seconds and then very light for 90 seconds. This pattern continues for 15-20 intervals. This may make you feel a little uncomfortable due to the exertion of exercise and potential for an increase in body temperature. This will mean that you are likely to sweat. As with any form of exercise there is a risk that you'll have a heart attack or stroke, but this is extremely unlikely in young, athletic people.

Cold Stress:
Cold stress does not pose a risk to healthy individuals. However, it is important to realize that this procedure will result in discomfort due to the decreases in your body temperature. This will make you feel cold, and it is possible that you may shiver. For your safety, this procedure will be terminated if you are too cold at any point in the cold conditions (internal temperature falls below 35.5°C or 95.9°F). Reaching these low body temperatures is highly unlikely but these safeguards reduce the level of discomfort that you may experience.

Lower Body Negative Pressure:

Dizziness, light-headedness, and feeling sick are common side effects. However, these are not always experienced. If you experience any of these, please let an investigator know and they will immediately stop the test. Additionally, the investigators will ask you how you are feeling throughout this test. Again, if you respond that you are not feeling OK, or report any side effects the test will be terminated. Additionally, the investigators will be monitoring you continuously throughout the test. If they note a decrease in blood pressure (to 80/50mmHg) or pronounced decrease in heart rate they will stop the test immediately. Upon termination of the test, you should begin to feel better almost immediately.

Internal temperature measurement: If the measurement of internal temperature is made via rectal probe/thermocouple there is a very small chance of infection. However, the probe is received sterile from the manufacturer and will remain that way until you open the packaging around the probe immediately prior to self-insertion. Alternatively, if you take the ingestible pill, there is a small risk that the pill you swallow to measure your internal body temperature will become stuck. However, to avoid the likelihood of this happening you are not allowed to be included in the study if you have a history of abdominal surgery. Additionally, this pill contains metal and because of this you will not be included in this study if you are scheduled for any sort of body scan within 7 days of taking the sensor, such as an MRI scan.

Maximal Skin Blood Flow: This procedure requires that a small patch of your skin, the size of a quarter dollar, is heated up for 30 minutes. It is possible that you will feel a very small discomfort in the area being heated up. If this happens, please notify the investigator. There is also an extremely small risk that the device heating your skin could malfunction. However, in order to protect you we will place a very fine temperature sensor underneath the device over the top of your skin. If the temperature of your skin in this area exceeds 43°C or 109.4°F we will stop the procedure immediately

Given that we are currently in the midst of the COVID-19 pandemic there may be an increased risk of infection to you in participating in this study given that you will spend time in a research laboratory with other research investigators whilst exercising. In order to mitigate the risk of exposure to COVID-19, the facemask or mouthpiece with nose clip ensemble will be fitted with a microbial filter. This is similar to those found in the facemasks many people have been wearing over their nose and mouth. Where possible, we will also instruct you to instrument yourself to minimize contact with study investigators, such as when placing the facemask or mouthpiece with nose clip. A thorough disinfection procedure will be employed prior to each study visit. That is, all hard surfaces will be sanitized while facemask or mouthpiece with nose clip ensembles will all be thoroughly cleaned and sterilized to ensure that the risk of exposure to COVID-19 is minimized. Investigators will wear medical gloves throughout.

**Benefits** This study is designed for the researcher to learn more about the role of exposure to cold conditions following exercise upon the ability of an individual to cope with blood loss. The findings of this study may be of benefit to soldiers, firefighters, construction workers and police offers, all of whom are at increased risk of experiencing injury and blood loss as part of their profession. Finally, you may be interested to know your exercise capacity. We will gain an insight into this in Visit A when we measure your maximal capacity to take in oxygen from the surrounding air and use it in your muscles to perform exercise ($VO_2$ Max).

**Compensation:** None

**Confidentiality**

You will be assigned a subject number so that the researchers can keep your personal information secret. One copy of the key that links your personal information to your subject number will be kept in Dr. Pearson's office in a locked cabinet. All of your collected data will be stored on computers and protected by passwords.

Your confidentiality will be maintained to the degree permitted by the technology used. Specifically, no guarantees can be made regarding the interception of data sent via the Internet by any third parties.

Certain offices and people other than the researchers may have access to study records. Government agencies and UCCS employees overseeing proper study conduct may look at your study records. These offices include the UCCS Institutional

Review Board, and the UCCS Office of Sponsored Programs and Research Integrity. UCCS will keep any research records confidential to the extent allowed by law. A study number rather than your name will be used on study records wherever possible. Study records may be subject to disclosure pursuant to a court order, subpoena, law or regulation.

Your de-identified data collected during this study could be used for future research studies without additional consent.

**Voluntary Participation and Withdrawal from the Study**

Taking part in this study is voluntary. You have the right *to* leave a study at any time without penalty. Withdrawal will not interfere with your future care or services at UCCS. You may refuse to do any procedures you do not feel comfortable with or answer any questions that you do not wish to answer. If you withdraw from the study, you may request that your research information not be used by contacting the Principal Investigator listed above and below.

**Contact Information**

Contact (PI's info): *jpearso5@uccs.edu*

- if you have any questions about this study or your part in it,
- if you have questions, concerns or complaints about the research, or
- if you would like information about the survey results when they are prepared.

Contact the Research Compliance Program Director at 719-255-3903 or via email at irb@uccs.edu:

- if you have questions about your rights as a research participant, or
- if you have questions, concerns or complaints about the research.

**Consent**

A copy of this consent form will be provided to you.

Are you interested in being contacted about future research I may conduct? ☐ Yes or ☐ No." »

I understand the above information and voluntarily consent to participate in the research. By signing this consent, I am confirming that I am 18 years of age or older.

Signature of Participant _____ Date _____