

**UC Riverside**  
**RESEARCH INFORMED CONSENT**

***Title of research study: The role of acetazolamide in mitigating inflammation and innate immune activation at high altitude: a randomized cross-over controlled trial***

***Investigator:***

PI:	Erica Heinrich, PhD, Assistant Professor Division of Biomedical Sciences, School of Medicine 951-827-9198 erica.heinrich@medsch.ucr.edu
Lead Researcher	Abel Vargas, PhD Candidate Division of Biomedical Sciences, School of Medicine 619-947-0610 avarg048@ucr.edu

***Funding:***

Wilderness Medical Society
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***Key Information about This Research Study***

This section provides highlights of this research study to help you decide whether or not you should participate. Carefully consider this information and the more detailed information provided below the section. Please ask questions about any of the information you do not understand before you decide whether to participate.

- **Purpose:** This is a research study about the effects of high-altitude travel on the immune system. The medication Acetazolamide will be used to treat hypoxemia and improve sleep quality at high altitude to determine if these factors influence changes in the immune system.
- **Procedures:** Participation in this study will involve travel to a high-altitude field site near Bishop, CA in two separate trips. It will also involve collecting biological samples including blood and urine. During each trip, you will be assigned to a treatment group (Acetazolamide or placebo) and will be asked to take this medication as instructed. It is expected that your participation will last 2-3 months, including six laboratory visits and two trips to the high-altitude field site, Barcroft Station.
- **Risks:** Risks of this study are significant. Some of the foreseeable risks or discomforts of your participation include the risk of Acute Mountain Sickness during high-altitude travel. Side effects of Acetazolamide use may include fatigue, abdominal pain, nausea, vomiting, and paresthesia. However, this medication is commonly prescribed for high-altitude travel.

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- **Benefits:** You may benefit from this research. Some of the benefits that may be expected include room and board for two 3-day stays at the Barcroft Field Station in the Eastern Sierra mountains.
- **Alternatives:** Your alternative to participating in this research study is to not participate.
- **Compensation:** You will be paid \$500 for your participation.
- **Voluntary Participation:** Your participation in this study is voluntary. You can decide to participate or not to participate, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled to or already have.

The remainder of this form contains a more complete description of this study.

### ***Purpose***

You are being asked to participate in a research study. This is a research study about the impact of high-altitude travel on the immune system and the impact of the drug, Acetazolamide/Diamox on these outcomes. This drug is FDA approved for the treatment of Acute Mountain Sickness (AMS). AMS is commonly experienced during travel to high altitude and may include symptoms such as headache, nausea, fatigue, dizziness, and difficulty sleeping. The study includes a double-blind placebo-controlled crossover design, which means that you will travel to high altitude twice and be assigned to take either Acetazolamide or placebo during each trip. Only the pharmacy team will know which treatment you are assigned to. Your treatment schedule will be shared with you at the end of the study.

The study researchers, Abel Vargas and Erica Heinrich from the UCR School of Medicine, or another approved research team member will explain this study to you.

You are being asked to take part in this study because you are a healthy volunteer with no history of cardiovascular or pulmonary disease, including prior high-altitude pulmonary edema (HAPE) or high-altitude cerebral edema (HACE), and you are not currently taking any anti-inflammatory medication or being otherwise treated for an inflammatory condition or infection.

### ***Investigator Financial Conflict of Interest***

No one on the study team has a disclosable financial interest related to this research project.

### ***What happens if I say yes, I want to be in this research?***

If you decide to participate in this research study, the researchers will ask you to:

- *Travel to a high-altitude site near Barcroft, California (Barcroft Field Station) during the Summer of 2025. Transportation will be provided to you and study members will travel by car in groups. All lodging and meals will be provided. More information about Barcroft Station can be found here: <https://www.wmrc.edu/barcroft-station/>*
- *Complete an initial visit to the laboratory at UC Riverside to complete baseline measurements and receive your assigned treatment. These measures include:*
  - *answering questions about your medical history and current symptoms*
  - *measurements of your height, weight, and abdominal circumference*
  - *a lung function test and breathing reflex test*

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- providing urine and blood samples.
- Take prescribed medication as instructed by the research team for 5-6 days at a time over two trips to high altitude. You will be provided with your assigned treatment/drug prior to each trip by a physician team member. You will be asked to take the treatment/drug twice per day (morning and evening), starting 2 days before the ascent to high altitude and each day at high altitude. You will not know if you are receiving Acetazolamide or a placebo during each trip.
- The overall schedule of testing is as follows:
  - Initial sea level visit at UC Riverside
  - Return to UC Riverside on the day of ascent for trip 1
  - Travel to Barcroft Station and remain for 3 days, then return
  - 1-week follow-up visit at UC Riverside
  - Return to UC Riverside on the day of ascent for trip 2 (approximately 30 days after return from trip 1)
  - Travel to Barcroft Station and remain for 3 days, then return
- Throughout the study, we will remain in contact with you via email and phone communication.
- During each trip to high altitude you will perform the following tests daily:
  - answering questions about your current symptoms
  - a lung function test and breathing reflex test
  - providing urine and blood samples.
- A total of 9 blood draws will occur over an approximately 2-month period. Each blood draw will be less than 25 ml total (225 ml of blood total throughout the study). Blood samples will be used to evaluate any changes in the immune system and the molecular and epigenetic mechanisms underlying these changes. Leftover samples will be stored in the Heinrich Lab for use in related studies but will not be associated with any of your identifying information. Whole genome sequencing will not be performed. Clinically relevant research results, including individual research results, will not be disclosed to you.
- A total of 8 urine samples will be provided over an approximately 2-month period. Each sample will be less than 50 ml (up to 400 ml of blood total throughout the study). Urine samples will be used to evaluate your hydration status and kidney function. Leftover samples will be stored in the Heinrich Lab for use in related studies but will not be associated with any of your identifying information. Clinically relevant research results, including individual research results, will not be disclosed to you.
- Electrocardiogram (ECG): We will place surface probes on your skin on the chest and ask you to sit quietly and rest for several minutes.
- Blood pressure: An inflatable cuff will be placed on your upper arm and inflated then slowly deflated while we listen to blood flow in your arm with a stethoscope.
- Lung function test: You will be asked to take a deep inhale then exhale as fast and as much as possible into a mouthpiece.
- Breathing reflex test: You will complete a breathing test in which you will sit with a mask covering your mouth and nose while you breathe different concentrations of nitrogen, oxygen, and carbon dioxide. During this test you will be fitted with an ECG and a finger pulse oximeter to measure your heart rate and oxygen saturation.

- **Study location:** All these procedures will be done at the UCR laboratory in the School of Medicine Research Building, room 120 and 130, or at Barcroft Field Station in the White Mountain Research Center. The research procedures at Barcroft Station will take place in dedicated private, space equipped for our research procedures.

### ***Is there any way being in this study could be bad for me?***

Participating in this research study may involve risks or discomforts that include:

- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort or the needle stick may hurt. There is a small risk of bruising and fainting, and a rare risk of infection.
- **Unexpected findings risks:** The EKG, blood draw, and breathing test are done for research purposes only. These measurements are designed to answer research questions, not to medically examine you or provide a clinical diagnosis. The EKG, blood draw, and breathing test are not a substitute for one a physician would order. They may not show problems that would be picked up by a medical EKG, blood draw, or breathing test. The researchers are not professionally qualified to act as your medical provider. However, if we see something unusual in your scan, we will inform you so that you can obtain appropriate follow-up evaluation by your physician. We will also provide you or your physician with a copy of the scan results upon request. Any follow-up evaluation or treatment that you seek will be at your own expense. Even if your physician rules out any problems, you may be unnecessarily worried if a problem is suspected.
- **High altitude and breathing test risks:** During the breathing tests, and at high altitude, you may experience some symptoms of acute mountain sickness (AMS) including lightheadedness or headache. Travel to high altitude can sometimes also decrease sleep quality and may cause temporary nausea in some participants. All of these risks are possible on any recreational trip to high altitude. If you experience a severe headache, you will be allowed to take ibuprofen and may be given supplemental oxygen to breathe through a nasal cannula. To minimize the risk of AMS symptoms, participants should remain hydrated and should not to engage in strenuous physical activity on the first day at altitude.
- **Use of an inactive intervention (placebo) risks:** All risks associated with high altitude travel described above may be experienced when assigned to the placebo treatment.
- **Travel:** Travel in a car includes the risk of traffic accident or vehicle break-down. Travel on a mountain road may also make some participants feel nervous.
- **Emotional risks:** During blood draw procedures, and while wearing the face mask, you may feel anxious or uncomfortable. Women who complete a urine pregnancy test may experience emotional stress in the event of an unexpected result.
- **Unknown risks:** The experimental measurements may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask the PI (see contact information above).

***Will being in this study help me in any way?***

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits to you include the opportunity to visit the White Mountain Research Center and surrounding national forests. This research may help others by providing new knowledge about how hypoxia impacts the immune system in clinical conditions such as lung disease and acute infections.

***What happens to the information collected for the research?***

Information [and/or specimens] collected for this research will be de-identified and coded with an ID number. Electronic documents will be encrypted and stored on the UCR School of Medicine secure server. Paper documents will be stored in a locked file cabinet in Dr. Heinrich's office in the School of Medicine Research Building, which always requires key-card access. Documents containing your name and contact information will be destroyed at the end of the study (approximately 2 years after collection). If you request to be contacted for future studies at the end of this document, your name, email, and phone number will be stored in a separate secure document for communication purposes only, and will not be associated with any of your study data or specimens. De-identified data and biospecimens will be stored indefinitely and may be used for future related research. If you choose to withdraw from the study, all electronic and paper documents containing your data will be destroyed. If you choose to withdraw after your identifying information has been destroyed, it may no longer be possible to identify your samples and data for destruction.

Identifiers might be removed from the identifiable private information. After such removal, the information could be used for future research studies or distributed to other investigators for future research studies without additional informed consent from the subject or the legally authorized representative.

***Will information about me be kept private?***

We will do our best to make sure that the personal information gathered for this study is kept private. However, we cannot guarantee total privacy and if required by the law, your personal information may be disclosed. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. However, if you consent to be photographed at the end of this document, photos from the study including your image may be used for scientific presentations related to this work. Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- The Institutional Review Board (IRB) that reviewed this research
- Representatives of the Sponsor (Wilderness Medical Society)
- Representatives of the University of California

***Can I be removed from the study without my OK?***

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include not following instructions

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from the research team, reporting severe or unusual symptoms, or no longer meeting study inclusion criteria. The researcher will notify you if this occurs.

### ***Can I stop being in the study at any time?***

You can stop taking part in the study at any time. If you would like to stop, please immediately contact the study PI or Lead Researcher (see contact information at the beginning of this document).

### ***Will I receive payment for being in this study?***

If you agree to take part in this research study, we will compensate you \$500 for your time and effort. If you complete only one half of the study (one trip to high altitude) you will receive \$250. If you complete only the initial sea level visit, you will receive \$50. Payment will be provided to you in person in the form of cash or Visa gift card at the end of the study or when you choose to withdraw.

Please notify the research team if you require a parking pass during visits to the UCR campus and one will be provided for you.

The results of this study may have commercial value to the sponsors, UC Riverside, and/or the researchers. Please know you will have no legal or financial interest in any commercial development resulting from the research or from the information or materials collected.

### ***What else do I need to know?***

If you get injured as a direct result of being in this study, the UC Riverside will provide reasonably necessary medical treatment, if it is available at that location. You can also seek medical treatment at a non-UC facility. Who pays for the treatment depends on different factors. The costs of medically necessary treatment may be handled in one of the following ways:

1. The costs may be covered by the University of California (for example, this may occur if you receive treatment at a University of California facility),
2. The costs may be billed to you or billed to your insurer, just like other medical costs, or
3. The costs may be covered or reimbursed by the University.

The University do not normally provide any other form of compensation for injury. For more information, visit [risk@ucr.edu](mailto:risk@ucr.edu).

If you are interested in receiving the research results following completion of the study, please contact the lab at [physiology@medsch.ucr.edu](mailto:physiology@medsch.ucr.edu) or visit our website at [hypoxialab.ucr.edu](http://hypoxialab.ucr.edu) to see our latest publications.

### ***Whom can I talk to?***

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at [erica.heinrich@medsch.ucr.edu](mailto:erica.heinrich@medsch.ucr.edu).

If you have questions about your rights or complaints as a research subject, please contact the IRB Chairperson at (951) 827 - 4802 during business hours, or to contact them by email at [irb@ucr.edu](mailto:irb@ucr.edu).

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**CONSENT**

You have been given a copy of this consent form, and the Subject's Bill of Rights, to keep.

Participation in research is voluntary. The decision to participate, or not participate, is solely up to you. You have the right to decline to be in this study, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled to or already have.

If you wish to participate in this study, you should sign below.

\_\_\_\_\_  
Date

\_\_\_\_\_  
Participant's Name (Print)

\_\_\_\_\_  
Participant's Signature for Consent

The research team may take photographs during the study. These photos may be utilized in scientific presentations. Please specify below if you consent to be in photographs.

☐ Yes, I consent to be photographed

☐ No, I do not consent to be photographed

The research team may save your contact information for the purposes of recruiting for future studies. Please indicate below if you consent to have your contact information saved and to be contacted about future studies.

☐ Yes, I consent to be recontacted

☐ No, I do not consent to be recontacted

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