Principal Investigator: Ellen L. Burnham, MD
COMIRB No: 14-0630
Version Date: 04/15/2022
Version: Inpatient

Study Title: Effect of alcohol and drugs of abuse on immune function in critically ill patients with respiratory failure

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Key Information:

Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

You are being asked to be in a research study. Participation in research is voluntary.

Purpose of this study: The purpose of this study is to learn more about relationship of drug and alcohol use on lung infections, respiratory failure, and recovery from critical illness.

Procedures: While you were a patient in the ICU, you were enrolled in this study by the consent of your legally authorized representative while you were incapacitated by your condition. If you agree to participate, the following will happen:

- Blood, tissue, nasal epithelial brushing, urine, tracheal aspirate and/or lung fluid may have already been collected from you. These samples were collected as part of your routine care and leftover specimens were obtained for this research study. Data from your medical records and information from your legally authorized representative and other family members regarding social history may have already been collected as well.

If you agree to continue to participate, the following will happen:

- Data from the medical records and leftover clinical specimens will be collected. A walking assessment, Pulmonary Assessment involving a CT scan, Pulmonary Function Testing, and Neurocognitive Assessments (questionnaires) will be administered while you are in the hospital. You have the option to participate in a long-term follow-up portion of the study which lasts for 12 months with follow-up visits at 2 weeks, 3 months, 6 months, and 12 months. Each visit will last approximately 2-3 hours and may be done in person or via remote telehealth visits.

Risks: Participation in this study involves risks, including the following:

- Bruising, pain from blood draws; uncomfortable answering questionnaires; radiation from CT scan; lightheadedness or shortness of breath from lung function tests; mild discomfort from walk testing.

Benefits: There is no guarantee that your health will improve if you join this study. This study may lead to information that could help patients and health care providers in the future.

Detailed Consent:

While a patient within the ICU, you were incapacitated by your condition (you could not make medical decisions for yourself). Your enrollment in this research study was permitted in part by COMIRB (the organization that oversees research projects at the hospital according to Federal regulations), and in part by the consent of your legally authorized representative. Now that you have regained the ability to make your own medical and research participation decisions, we are asking you to consent to *continue* your participation in the study.

Your consent to continue to participate in this study is necessary if the researchers are to continue. If you refuse to continue to participate, you will be removed from the study, your samples will be no longer used, and all data and samples collected from you will be destroyed.

Why is this study being done?

This study plans to learn more about people who are sick in the hospital with a lung infection, and respiratory failure. Respiratory failure, or severe lung failure, is a life-threatening disease. When it happens, the lungs have trouble carrying out their normal function of getting oxygen into the blood and removing carbon dioxide from the body. We are also doing this study to see what drinking too much alcohol, using tobacco, or using drugs does to lung infections and respiratory failure. We also want to learn how alcohol use affects patients' mental processing as they recover from respiratory failure, including COVID-19.

You are being asked to be in this research study because you are admitted to the ICU and are receiving breathing support from a ventilator either due to a lung infection or respiratory failure. Alcohol, tobacco, and drug use have been linked to lung infections, respiratory failure, and even death, but the reasons for this aren't known. People who use unhealthy amounts of alcohol, tobacco and or drugs may be more at risk for lung infections, and for severe complications due to lung infection. Your participation is important whether or not you use alcohol, tobacco, and or drugs.

Certificate of Confidentiality

A Certificate of Confidentiality has been obtained from the Federal Government for this study to help insure your privacy. This Certificate means that the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. But, if you request disclosure, we can release the information.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects, or for information that must be disclose in order to meet the requirements of the federal Food and Drug Administration (FDA).

Other people in this study

Up to 300 people from your area will participate in the study.

What happens if I continue in this study?

You may have already had samples of blood, tissue, nasal epithelial brushing, urine, tracheal aspirate and/or lung fluid collected from you.

Data concerning your medical record together with ongoing testing and laboratory reports have been collected. We have noted the medicines you use, and those you are receiving in the hospital. In addition, we have collected biographical data about you, both from your medical record and from your medical decision maker and perhaps other family members. This data included a social history, and included any use of alcohol, cigarettes, and drugs (legal, prescription drugs or otherwise).

As a part of your care, the ICU physician or someone under his direction may have performed a procedure known as bronchoscopy with bronchoalveolar lavage (BAL). This procedure was performed by the ICU team as a part of your treatment or for diagnosis purposes. During this bronchoscopy, your doctor washed a segment of your lungs with sterile saline (lavage). The saline was suctioned from the lungs and sent to the hospital laboratory for analysis. There is often extra fluid left over, besides the amount needed for your regular care, and this extra fluid given to the research team.

If you did not have a bronchoscopy performed, a licensed respiratory therapist may have performed a tracheal aspirate as a part of your routine care. While you are receiving oxygen from the ventilator, a sterile catheter is inserted into the endotracheal tube (breathing tube) and approximately 1 tablespoon of sterile saline is placed inside and immediately aspirated (sucked back out) out of the breathing tube into a sterile container. Some of this sample was used as a part of your routine care, and the leftover portion was given to the research team. This will only occur once.

If you continue in the study, and even if you do have not had the bronchoscopy or tracheal aspirate procedures, you will continue to have some of your data and clinical samples collected. These are data and samples that will not have already been collected as part of your standard care. We would like to ask you questions about your use of alcohol, tobacco, and other drugs (both legal, prescription drugs and illegal drugs) using specialized questionnaires designed for this purpose. If we learn information that is important to your care but that is not already in your medical chart, we will alert your doctors but we will not share this information with anyone else. The surveys will take approximately 30 minutes to complete.

In addition, we will request your permission to keep some of the unused samples of lung fluid, tracheal aspirate, blood, nasal epithelial brushing, urine or tissue, as well as the data collected, for use in future research. This cannot be done without your consent.

After leaving the hospital, you will be invited to return to the outpatient study clinic for follow up visits at 2 weeks, 3 months, 6 months, and 12 months. Participation in long-

term follow up is optional. If you do not want to return for this longer-term follow up, the study team will retain data from your inpatient hospital portion of the study, and your participation will be completed at that point.

Each follow up visit will last approximately 2-3 hours. These visits may take place in person or via remote telehealth visits. The 2-week visit will be a telehealth visit.

Before beginning each in-person visit, we will check your alcohol level using a breath test to make sure it is safe for you to continue testing at the visit, followed by questions about regular alcohol use and whether you have been readmitted to the hospital. At the three- and six-month visits, we will then perform a blood draw, walk testing, neurocognitive and pulmonary assessments. At the 12-month visit, we will perform a blood draw, neurocognitive and pulmonary assessments. At each visit, we will collect approximately two tablespoons of blood, and three tablespoons of urine.

Walking Assessment: We will perform two different walking tests to test your muscle function. The first, the six-minute walk test, tests how far you can walk in six minutes. The second, the 4-meter gait speed test, tests how quickly you can walk 4 meters.

Pulmonary Assessments: We will perform a CT ("Cat Scan") scan of your chest. Similar to an x-ray, the CT scan involves exposure to a small amount of radiation, using the smallest amount possible. The CT scan will give us a three-dimensional picture of your lungs to help us determine if your lungs have healed from your previous infection, or if there is evidence of lung scars. For the CT scan, you will need to be able to lie flat for approximately 10 minutes in order for the test to be completed. It's possible that you may only have one CT scan performed, depending on the results of your first CT scan. The decision to repeat or not repeat the CT scan will be made by the study doctor and discussed with you.

Pulmonary Function Testing (PFTs): the pulmonary function test is a breathing test that measures how fast air moves in and out the lungs. This will show us that your lungs work normally. It's possible that you may only complete one set of Pulmonary Function tests (PFTs), depending on the results of your first set. The decision to repeat or not repeat the Pulmonary Function tests will be made by the study doctor and discussed with you.

Neurocognitive Assessments: At each visit, we will ask you detailed questionnaires regarding your nutritional status, breathing status, alcohol use and home situation. We will ask other questions about delirium experienced during your hospital stay, depression, stress, anxiety and your quality of life. Based on your responses to these questions, you may be asked to participate in assessments to further understand lasting effects of delirium experienced during critical illness. A psychiatrist with experience assessing patients following critical illness, will perform these assessments.

Medical chart review: We will get information about your health from your medical record from your date of admission throughout the course of your hospital stay until hospital discharge, and possibly up to 12 months after you leave the hospital. This information will include information about your acute illness, laboratory tests, x-rays,

pulmonary function tests, and prior medical history. The medical record will be used to access information about the care you receive in the hospital and ICU. Also, if you receive outpatient, clinical care at the University of Colorado Hospital, ICU Recovery Clinic, we will review your chart to see how much you have recovered at 12 months.

Please ***initial*** below next to the statement which states your preference about participating in the long-term follow up portion of the study.

_____☐ I agree to participate in long-term follow up at 2 weeks, 3 months, 6 months, and 12 months post-hospitalization.

_____☐ I do not wish to participate in the long-term follow up portion of the study.

What are the possible discomforts or risks?

The risks of nasal brushings include eye tearing, runny nose, and bleeding from the nose.

Risks of Having Blood Taken

Approximately two tablespoons of blood will be drawn at three timepoints during your hospital stay and at each optional follow up visit after discharge. If you complete all six visits, the total amount of blood to be collected will be twelve tablespoons of blood over twelve months. For the blood samples, we will take blood from catheters/intravenous (IV) lines that are already in place and at the time of your other laboratory tests if possible. When no catheter or IV is available from which to draw blood, we will get blood by putting a needle into one of your veins and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin.

Completing questionnaires and neurocognitive assessments related to stress, anxiety, alcohol, tobacco, and drug use may cause discomfort to some people. If we discover that you have a problem with alcohol or drug use, we can help you with names and telephone numbers of agencies that may help alleviate your concerns or may be able to address your needs.

There is a small chance that you could become uncomfortable answering our questions. You may decline to answer any question(s) that you do not want to answer. Also, if you suffer from any psychological distress including but not limited to symptoms of anxiety, depression, or posttraumatic stress, it is possible that you may experience psychological discomfort with some of the survey questions. You may share these feelings with the study team, who will provide you with contact information at the beginning of the study. A handout with additional external mental health resources will also be provided. A mental health care referral may also be provided.

You may experience some shortness of breath with walk testing and this is a sign that you should take a rest.

As part of this study, we will perform a CT scan of your chest. CT is a way of taking

detailed pictures inside your body by using X-rays. X-rays are a type of radiation.

You get some radiation from your environment. You get radiation from bricks and concrete, from some foods, and from radon gas, which is an invisible gas that seeps out of the ground. The amount of radiation that this CT scan will deliver to your body (give you) is about the same as you would get from living in your environment for **3 years**.

This is an estimate. The amount of radiation you get could be higher or lower, depending on the machine, the power setting, and your body weight. Exposure to radiation at high levels increases a risk of developing cancer. There is no evidence of such risks for diagnostic procedures. **The risk of this procedure is not equal for everyone. The risk is much higher for unborn babies if the mother has this procedure. The risk is also much higher for young children and teenagers. The risk is much lower for people over the age of 30.**

Risks from pulmonary function testing**:** You may experience a feeling of lightheadedness from breathing through the spirometry tubing. Also, there is a very rare but serious risk of a collapsed lung (less than 1%).
Other possible risks include a risk of discovering information during the research project that may have an effect on your later health (uncommon but serious). If we discover that you have an underlying medical disorder, we can help you with referrals to appropriate health care providers that may be able to address your needs.

There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

What are the possible benefits of the study?

This study is designed for the researchers to learn more about the relationship of alcohol, tobacco, and other drug use on lung infections, respiratory failure, and recovery from critical illness. This study is not designed to treat any illness or to improve your health. It is possible that the CT scan or other study procedures may uncover an illness or disease where different therapies may be helpful. If this occurs, the study team will provide this information to you and your doctors.

If you decide to take part in this study, there is no promise that your health will improve. Also, there may be risks, as discussed in the section describing the discomforts or risks.

Are there alternative treatments?
You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you.

Who is paying for this study?

This research is being sponsored by the National Institutes of Health (NIH). The sponsor (NIH) will only pay for procedures not considered standard of care, as detailed below.

Will I be paid for being in the study?

There is no payment for the study visits during your inpatient hospital stay.

If you participate in the optional outpatient follow up visits, you will be paid for study visits that you complete as follows:

- Two-week Tele-Health visit: $25.00.
- 3-month clinic visit: $50.00.
- 6-month visit: $75.00.
- 12-month visit: $100.00.

PFTs: Each time you complete full PFTs for the study, you will be paid $25.00, up to $75.00 total if all three outpatient tests completed.

CT scan: Each time you complete a CT scan for the study, you will be paid $25.00, up to $75.00 total if all three outpatient tests completed.

Each payment will be in the form of an electronic gift card sent to your email. If you do not have an email address, you may receive a Visa gift card.

If you complete all study follow-up visits and all PFTs and CT scans, you will be paid $400.00 total.

If you do not complete all follow up study visits, leave the study early, or if we must remove you from the study, you will be paid only for the visits and tests you have completed.

Will I have to pay for anything?

It will not cost you anything to be in the study.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study. Ask your study doctor.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the sponsor may stop the study at any time.

What happens if I am injured or hurt during the study?

If you have an injury while you are in this study, you should call Ellen Burnham, MD

immediately. Her phone number is 303-724-6078.

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is Ellen Burnham, MD. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Ellen Burnham, MD at 303-724-6078. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Ellen Burnham, MD with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

Optional Consent and Authorization for Specimen Banking for Future Research.

Dr. Ellen Burnham would like to keep some of the blood, nasal epithelial brushing, urine, tracheal aspirate, and bronchoscopy samples taken during the study but not already used for other tests. If you agree, the samples will be kept and may be used in future research to learn more about lung diseases and other diseases or conditions. The research that is done with your samples is not designed to specifically help you. It might help people who have lung diseases, and other diseases, in the future. Reports about research done with your samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your samples will not affect your care.

The choice to let Dr. Burnham keep the samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time, and contact Dr. Burnham to let her know that you do not want her to use your samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Burnham decides to destroy them.

When your samples are given to other researchers in the future, Dr. Burnham will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes samples are used for genetic research (research about diseases that are passed on in families). Even if your samples are used for this kind of research, the results will not be told to you, and will not be put in your health records. Your samples will only be used for research and will not be sold. The research done with your samples may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your samples include learning more about what causes lung disease and other diseases, how to prevent them, and how to treat them. The greatest risk to you is the release of your private information. Dr. Burnham will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no

cost to you for any sample collection and storage by Dr. Burnham.

I give my permission for my data, blood and tissue to be stored in a central tissue bank at the University of Colorado Denver, for future use by the study investigators:

1. I give my permission for my data, blood, tissue and lung fluid/aspirate samples to be kept by Dr. Burnham for use in future research to learn more about how to prevent, detect, or treat lung diseases.

   _____YES _____NO _____Initials

2. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

   _____YES _____NO _____Initials

3. I give my permission for my data, blood, tissue, and lung fluid/aspirate samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

   _____YES _____NO _____Initials

I agree to take part in the study having to do with research on blood and tissue as indicated above.

Who will see my research information?

The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include

- University of Colorado Denver
- University of Colorado Hospital

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your

permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Ellen L. Burnham, MD
University of Colorado School of Medicine
12700 E 19th St., Mailstop C272
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:.

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- The NIH, who is paying for this research study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we followall of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator.

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, email address, location of birth). Your name, phone number and email address will be kept separate from research specimens and data
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Alcoholism, Alcohol or Drug abuse
- Tissue samples and the data with the samples.

What happens to Data, Tissue, Blood and Specimens that are collected in this study?

Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures of disease. The data, tissue, blood and specimens collected from you during this study are important to this study and to future research. If

you join this study:

- The data, tissue, blood, or other specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

HIPAA Authorization for Optional Additional Study Procedures – In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:

_____I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

Agreement to be in this study and to use my data

I have read this paper about the study, or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use, and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study; I will get a signed and dated copy of this consent form.

Subject Printed Name:_____

Subject Signature:_____ Date:_____

Study Personnel explaining Consent (printed name):_____

Date:_____

Study personnel Signature:_____

Study Personnel Role/Title:_____

Witness:_____ Date_____

Witness Printed Name: _____

Witness of Signature ☐ Witness of consent process ☐