Official title: Vitamin C Infusion for TReatment in Sepsis and Alcoholic Hepatitis

NCT #: 0829683

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# RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

**STUDY TITLE:** Vitamin **C** **I**nfusion for **TR**eatment **I**n **S**epsis and **A**lcoholic **H**epatitis **(CITRIS – AH)**

**VCU INVESTIGATOR: Arun J. Sanyal MD and Alpha A. Fowler, MD**

**SPONSOR: National Institute on Alcohol Abuse and Alcoholism**

*NOTE: In this consent form, "you" always refers to the research participant. If you are a legally authorized representative, please remember that "you" refers to the study participant.*

## ABOUT THIS CONSENT FORM

You are being invited to participate in a research study. **It is important that you carefully think about whether being in this study is right for you and your situation.**

This consent form is meant to assist you in thinking about whether or not you want to be in this study. **Please ask the study doctor or the study staff to explain any information in this consent document that is not clear to you.**

Your participation is voluntary. You may decide to not participate in this study. If you do participate, you may withdraw from the study at any time. Your decision not to take part or to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

## AN OVERVIEW OF THE STUDY AND KEY INFORMATION

The purpose of this research study is to test the safety, tolerability, and effectiveness of the Vitamin C (ascorbic acid) when used to treat alcoholic hepatitis (inflammation of the liver from heavy alcohol use) and sepsis (life-threatening complication of an infection). You are being asked to participate in this study because you have been diagnosed with alcoholic hepatitis and sepsis, and may meet the study entry requirements.

Alcoholic hepatitis is inflammation of the liver due to alcohol consumption. It can cause one or more of the following symptoms such as jaundice (yellow discoloration of the eyes and skin), pain on the right side of the abdomen, and is accompanied by an enlarged liver. As the body tries to fight an infection it sends chemicals into the bloodstream. These chemicals that are trying to fight the infection can cause inflammation. This inflammation can cause damage to many body systems and make them fail. Patients with alcoholic hepatitis and sepsis have low levels of Vitamin C in the bloodstream. Vitamin C has been shown to reduce inflammation and organ dysfunction in patients with severe infections. We do not yet know if Vitamin C will be effective in alcoholic hepatitis.

Taking Vitamin C by mouth is not effective as a treatment in people with your condition so you will receive the Vitamin C through your intravenous (IV).

In this study, you will be randomly assigned (like the flip of a coin) to receive either Vitamin C or a placebo (a look-alike inactive substance, a "sugar-pill" but in this case will be sugar water, or 50 mL of 5% dextrose in sterile water) given through your IV every six hours for four days. You have an equal or 50% chance of being assigned to one of the two groups. No one will know which group you will be in, including your doctors and nurses. This is done so at a fair evaluation of results may be made. Your doctor will be able to get this information if there is an emergency and believes that knowing which group you are in is necessary.

Also in this study, you will have the following done:

1. Have your blood drawn on day 0, 1, 2, 4, and 7
2. Assessments physical examination/EKG completed
3. Laboratory tests
4. We will collect information about health history, treatment notes, discharge summary
5. Screening procedures
6. Female participants will have a pregnancy test performed
7. Drug screening

Your participation in this study will last up to 90 days. Approximately 20 individuals will participate in this study.

This study will not use your samples to sequence all or part of your DNA.

Your alternative is to not participate in this study. You do not have to be in this study to be treated for your illness or condition. You will get the usual treatment even if you choose not to be in this study.

There are both risks and benefits of participating in research studies. We want you to know about a few key risks right now. We will give you more information in the "WHAT RISKS AND DISCOMFORTS CAN I EXPECT FROM BEING IN THE STUDY?" section.

| **Most Common Risks and Discomforts** | **Benefits to You and Others** |
|---|---|
| 1. There is a risk that study drug may not be as good as the usual approach for alcoholic hepatitis and sepsis<br>2. There is also a risk that you could have side effects from taking study drug. Below are some of the most common side effects:<br>• Dry Mouth<br>• Nausea<br>• Vomiting<br>• Dizziness<br>• Headache<br>3. There may be some risks to you that the study doctors do not know about yet, so | There is no guarantee that you will receive any medical benefits from being in this study. However possible benefits include reduced organ dysfunction and increased likelihood of survival. We hope the information learned from this study will provide more information about alcoholic hepatitis and sepsis. |

| | |
|---|---|
| we will let you know of any new findings.<br><br>4. Blood draws may cause pain, bleeding, and/or bruising. You may faint and could develop an infection at the site where blood is drawn.<br><br>5. Participation in research might involve some loss of privacy. There is a small risk that someone outside the research study could see and misuse information about you. This risk will be minimized by keeping all your research related information in a secure electronic server protected by VCU information technology firewalls that are state of the art. Also, your paper records will be kept in a secure location in the office of the research coordinator. | |

In general, we will not give you any individual results from the study. If we find something of medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

**Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask the study staff.**

## WHAT WILL HAPPEN IF I PARTICIPATE IN THE STUDY?

If you qualify for the study, you will be given study drug and will be randomly assigned (like the flip of a coin) to receive either Vitamin C or placebo. You have an equal chance of being assigned to any one of the groups.

Neither you nor the study doctor will know which study drug you are receiving. This information is available to the study doctor if needed in an emergency. This is called blinding, and it is done so that a fair evaluation of results may be made.

You will receive the Vitamin C or placebo through your existing IV every six hours for 96 hours (four days). If the IVs you currently have are not available to infuse the Vitamin C, because they are being used to give you medications for your clinical care, you may receive an additional IV. You would only receive an additional IV if the Vitamin C cannot be infused at the same time as the medications you are receiving to treat your condition. It is not likely that this will happen as Vitamin C may safely be infused at the same time as most other IV medications. The hospital pharmacist will determine if the Vitamin C may be infused at the same time as the medications you are receiving to treat your condition. You will have an electrocardiogram (ECG), where

sticky pads will be placed on your chest and a machine will trace the electrical activity of your heart, on day 2 and day 4.

About 1 to 2 tablespoons of blood will be collected at four different time points, on day 1, day 2, day 4, and day 7 for the purposes of this study. The samples will be obtained from your IV that you will have even if you are not a part of this study. This blood will be used to monitor certain substances in your blood as you receive the Vitamin C. These substances are called biomarkers and provide information about infection and inflammation. We will monitor how the Vitamin C affects the levels of these biomarkers. After we collect the blood for information about the biomarkers we will freeze it and store it until the entire study is completed. Once the study is completed, your blood samples will be analyzed. It is anticipated that only half of the blood we collected from you will be required to get the information we need. The other half will only be used for this study if something went wrong while processing the first half. If the second half of your blood sample is not needed, you will have the opportunity to allow that sample to be used for future research. If blood is drawn as part of your treatment that is also needed for this research, we will not draw extra blood. Instead, we will use the results of the blood work taken for your treatment. Most of the information we will collect about you will be in your medical chart as part of your regular treatment, which you will continue to receive whether or not you participate in this study.

## WHAT RISKS AND DISCOMFORTS COULD I EXPERIENCE FROM BEING IN THE STUDY?

Your condition may not get better or may become worse while you are in this study.

**Possible Risks Associated with Vitamin C:**

Although no harmful side effects of infused Vitamin C have been seen in previous studies, an allergic reaction is possible.

Occasional (Between a 1-10% chance that this will happen)

- Dry mouth
- Nausea
- Vomiting
- Dizziness
- Headache

Rare (Less than a 1% chance that this will happen)

- Allergic reaction to Vitamin C is possible, but rare. Severe allergic reactions can be life threatening.
- Development of kidney stones (oxalate nephropathy)
- Hemolysis related to glucose-6-phosphate deficiency (G6PD)

**Point of Care Glucose Testing**

Your blood sugar level will be tested daily while you are in the hospital, whether or not you participate in this study. Vitamin C can sometimes make the results of the finger-stick blood sugar testing method inaccurate. Therefore, while you are receiving study drug, we will monitor blood sugar levels by using the result from the main laboratory.

If you require injections of insulin or a continuous infusion of insulin to control your blood sugar, we will have to draw your blood more frequently to test your blood sugar levels. When we draw blood and send it to the laboratory we take more blood than if we were using the finger-stick method to test your blood sugar. At worst, we could take as much as 4-6 additional tablespoons of your blood in a 24-hour time period and that this could last for as many as seven days. It is also possible that we won't need to take this much blood. Each blood draw is approximately 1 teaspoon.

We will monitor everyone's blood this way for three days after your last infusion. This will allow the Vitamin C in your blood to return to a level that will not interfere with the finger-stick method of testing your blood sugar.

**Non-Physical Risks**
Participation in research might involve some loss of privacy. There is a small risk that someone outside the research study could see and misuse information about you.

**Unknown or Unforeseeable Risks**
The researchers will let you know about any significant new findings (such as additional risks or discomforts) that might make you change your mind about participating in the study.

**Reproductive Risk**
As the study procedures might injure an unborn child, pregnant women may not participate. Women who might become pregnant should use a medically accepted form of birth control such as total abstinence, birth control pills, an IUD, diaphragm, progesterone injections or implants, or condoms plus a spermicide. Methods of birth control other than total abstinence are not 100% effective, and should a woman become pregnant there is a risk of injury to an unborn child. For similar reasons, women who are nursing an infant may not participate.

## WHAT ARE THE COSTS?

Study drug will be provided by the sponsor at no cost to you. You will not be charged for any study visits, tests, or procedures.

You and your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your condition. This includes:

- The costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and to prevent and treat side effects.
- Your insurance co-pays and deductibles.

## WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THE STUDY?

If you are injured by, or become ill, from participating in this study, please contact your study doctor immediately. Medical treatment is available at the Virginia Commonwealth University Health System (VCU Health System). Your study doctor will arrange for short-term emergency care at the VCU Health System or for a referral if it is needed.

Fees for such treatment may be billed to you or to appropriate third party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study. To help avoid research-related injury or illness, it is very important to follow all study directions.

## CAN I STOP BEING IN THE STUDY?

You can stop being in this research study at any time, but the data collected on you to this point remains as part of the study database and cannot be removed. Leaving the study will not affect your medical care, employment status, or academic standing at VCU or VCU Health. Tell the study staff if you are thinking about stopping or decide to stop.

## HOW WILL INFORMATION ABOUT ME BE PROTECTED?

VCU and the VCU Health System have established secure research databases and computer systems to store information and to help with monitoring and oversight of research. Your information may be kept in these databases but are only accessible to individuals working on this study or authorized individuals who have access for specific research related tasks.

Identifiable information in these databases are not released outside VCU unless stated in this consent or required by law. Although results of this research may be presented at meetings or in publications, identifiable personal information about participants will not be disclosed.

Personal information about you might be shared with or copied by authorized representatives from the following organizations for the purposes of managing, monitoring and overseeing this study:

- The study Sponsor, representatives of the sponsor and other collaborating organizations
- Representatives of VCU and the VCU Health System
- Officials of the Department of Health and Human Services or the Federal Food and Drug Administration

It will be noted in your protected electronic medical record at VCU Health System that you are in this study. Information about the study, including any medications you may receive, will be noted in the record. This information is protected just as any of your other medical records are protected.

In general, we will not give you any individual results from the study. If we find something of medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Web site at anytime.

Your blood sample will also be tested for hepatitis and HIV. Virginia state law requires the study staff to report the results of positive tests for hepatitis and HIV to a local health agency.

There are no plans to share any money or profits with you if the use of your sample(s) results in inventions or discoveries that have commercial value.

**Future Research Studies**
In the future, identifiers might be removed from the information and samples you provide in this study, and after that removal, the information/samples could be used for other research studies by this study team or another researcher without asking you for additional consent.

**Certificate of Confidentiality**
To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, 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. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

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 disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

## HOW WILL MY HEALTH INFORMATION BE USED AND SHARED DURING THIS STUDY?

As part of this research study, we will ask you to share identifiable health information with us and/or permit us to access existing information from your healthcare records. New health information may also be created from study-related tests, procedures, visits, and/or questionnaires. This type of information is considered "Protected Health Information" that is protected by federal law.

**What type of health information will be used or shared with others during this research?**
The following types of information may be used for the conduct of this research:

| | | |
|---|---|---|
| ☒ Complete health record | ☒ Diagnosis & treatment codes | ☒ Discharge summary |
| ☒ History and physical exam | ☒ Consultation reports | ☒ Progress notes |
| ☒ Laboratory test results | ☒ X-ray reports | ☒ X-ray films / images |
| ☐ Photographs, videotapes | ☐ Complete billing record | ☐ Itemized bill |

☒ Information about drug or alcohol abuse ☒ Information about Hepatitis B or C tests
☐ Information about mental health ☐ Information about sexually transmitted diseases
☐ Other physical or mental health information (specify):

**Who will use or share protected health information about me?**
VCU and VCU Health are required by law to protect your identifiable health information. By consenting to this study, you authorize VCU/VCU Health to use and/or share your health information for this research. The health information listed above may be used by and/or shared with the following people and groups to conduct, monitor, and oversee the research:

- Principal Investigator and Research Staff
- Health Care Providers at VCU Health
- Institutional Review Boards
- Government/Health Agencies
- Others as Required by Law
- Study Sponsor
- Data Coordinators
- Data Safety Monitoring Boards

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

**When will this authorization (permission) to use my protected health information expire?**
This research study involves the use of a Data Registry or Sample Repository and will never expire.

**Statement of Privacy Rights**
You may change your mind and revoke (take back) the right to use your protected health information at any time. However, even if you revoke this authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization you may no longer be allowed to participate in the research study. To revoke this Authorization, you must write to the Principal Investigator.

## OPTIONAL STORAGE FOR FUTURE RESEARCH STUDIES

To advance science, it is helpful for researchers to share information. They do this by putting data or samples into one or more scientific databases (called registries or repositories), where it is stored along with information from other studies. Researchers can then study the information in other ways and combine information from many studies to learn even more about health and disease.

Your samples and/or health information will be stored by NIH/NIAAA in one or more scientific databases, and shared with other researchers. The samples and information will be available for any research question, such as research to understand what causes certain diseases (for example heart disease, cancer, or psychiatric disorders), development of new scientific methods, or the study of where different groups of people may have come from. This information will not be labeled with your name or other information that could be used to easily identify you. However, it is possible that the information, when combined with information from other public sources could be used to identify you, though we believe it is

unlikely that this will happen. Since this information will not contain personal information, it cannot be removed in the future and will be stored indefinitely.

**Permission to Store Data and/or Samples for Future Research Studies**
*Please circle your answer:* I agree that my data/samples may be stored and used for future research as described above.

YES NO

## WHO SHOULD I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY?

If you have any questions, complaints, or concerns about your participation in this research, contact:

Dr. Arun Sanyal
VCU Medical Center
1200 East Broad Street
Room 1490
Box 980341
Richmond, VA 23298
804-828-4060, 24 hours 7days/week.

The researcher/study staff named above is the best person(s) to call for questions about your participation in this study.

If you have general questions about your rights as a participant in this or any other research, you may contact:

Virginia Commonwealth University Office of Research
800 East Leigh Street, Suite 3000
Box 980568
Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number to ask general questions, to obtain information or offer input, and to express concerns or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk to someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

## STATEMENT OF CONSENT

I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered. By signing this consent form, I have not waived any of the legal rights or benefits to which I otherwise would be

entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form for my records.

| **Signature Block for Enrolling Adult Participants** | |
|---|---|
| _____<br>Adult Participant Name (Printed) | |
| _____<br>Adult Participant's Signature | _____<br>Date |
| _____<br>Name of Person Conducting Consent Discussion (Printed) | |
| _____<br>Signature of Person Conducting Consent Discussion | _____<br>Date |
| _____<br>Principal Investigator Signature (if different from above) | _____<br>Date |

| **Signature Block for Enrolling Decisionally Impaired Adult Participants – LAR Consent** | |
|---|---|
| _____<br>Name of Adult Participant (Printed) | |
| _____<br>Name of Legally Authorized Representative (Printed) | _____<br>Relationship to Participant |
| _____<br>Legally Authorized Representative Signature | _____<br>Date |
| _____<br>Name of Person Conducting Consent/Assent Discussion (Printed) | |
| _____<br>Signature of Person Conducting Consent/Assent Discussion | _____<br>Date |
| _____<br>Principal Investigator Signature (if different from above)<br>Date | _____<br>Date |