The University Of Texas Southwestern Medical Center At Dallas
Parkland Health & Hospital System

CONSENT TO PARTICIPATE IN RESEARCH

Acute Liver Failure/Acute Liver Injury

TITLE OF RESEARCH: A Multi-Center Group to Study Acute Liver Failure

SPONSOR: U.S. National Institutes of Health (NIH), the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)

INVESTIGATORS:	Telephone No. (regular office hours)	Telephone No. (other times)
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You may call these study doctors or research personnel during regular office hours at 214-645-6111. At other times, you may call them at 214-645-0595.

Instructions:

When we say “You” in this consent form, we mean you and/or your relative. Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?

Dr. William Lee from UT Southwestern Medical Center is conducting a research study among patients who develop acute liver Injury (ALI) or acute liver failure. The main

purpose of this study is to obtain information about the course of disease, samples of blood, urineand possibly tissue from patients with ALI or ALF. ALI isa severe and occasionally fatal condition in which liver cell damage leads to a serious illness requiring hospitalization. ALF is a severe and often fatal condition in which liver cell damage leads to a devastating illness and, frequently death. This study at UT Southwestern is part of a national study to gather clinical data, tissue, urine and blood samples on patients with this relatively rare condition.

Blood and urine collection is for the purpose of obtaining more information concerning the cause and the treatment of this illness. Since, in many instances, the cause of liver damage is not known, these samples will allow researchers to determine whether viruses or poisons of some kind have affected the liver leading to its failure to function.
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We do not fully understand the long-term course of this disease as there is little information collected to date. So we also wish to collect follow-up information at day 21, 6 and 12 months after you first enroll into the study. This is to study the possibility of long-term problems that might remain as a resulting from your ALI or ALF at 1 year after entering the study. . ***Why am I being asked to take part in this research study?***
If you have been diagnosed with acute liver injury, you are being asked to take part in this research study because this condition comes on rapidly and has a variety of causes including drugs, viruses and some genetic conditions. You may therefore be eligible to participate in this research study that is intended to improve our understanding of this condition and to help develop possible treatment for it.

If you have been diagnosed with acute liver failure, you are being asked to take part in this research study because this condition affects mental functioning and might impair judgment, you are being asked to provide informed consent for your relative.

In order to take part in this study you must have:

1) ALI without mental status changes with a tendency towards bleeding and/or

2) ALF with sudden onset of mental status changes and a tendency towards bleeding.

How many people will take part in this study?
About 200 people will take part in this study at UT Southwestern or Parkland Health & Hospital System, This study is also taking place at a number of other medical facilities around the country. There will be a total of 3,000 people participating in this research study throughout the United States and/or other countries.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form. Dr. William Lee or his designee will explain the study and this consent form in

detail and you will be given the opportunity to ask any questions you may have.

This study does not involve any treatment or intervention for any symptoms.
After you sign the consent form, you will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

Procedures and Evaluations during the Research:

Screening Procedures
To help decide if your family member qualify to be in this study, the researchers may ask you questions about his/her health, including medications he/she has taken and any surgical procedures he/she may have had.

He/she may also have to the following exams, tests or procedures completed as standard of care documented by the researcher:

- Physical exam and medical history;
- Vital signs;
- Blood tests;
- Electrocardiogram (EKG), a tracing of the electrical activity of the heart; and
- Demographic information (age, sex, ethnic origin).

Procedures and Evaluations during the Research
In general, clinical and laboratory parameters in the intensive care unit are measured twice daily. The data collection for the study is the Case Report Form. The information gathered are demographic and clinical data regarding the hospitalization for the liver disease.

Liver Biopsy: If you undergo a liver biopsy as part of your standard of care, you will be asked to provide the study team with a small portion of the liver tissue removed from the biopsy for future research purposes. You will only be asked to provide a liver tissue sample if you are already getting a liver biopsy based on the standard of care you are being provided by your physician.

Blood and Urine Samples: The only request presented here is that we be allowed to obtain an extra two tablespoons of blood from your relative each morning and a one-time collection of urine during seven days of your hospitalization for the purpose of obtaining more information concerning the cause and the treatment of this condition.

Follow up visits
You or your relative will be contacted at day 21 post enrollment into the study by phone or email to determine your overall health status and to plan future follow up visits. In addition, you will be contacted at months 6 and12 after your enrollment in this study for

a follow-up study visit. This visit can be completed by phone, email or in person at a clinic visit. Information about his or her current state of health will be collected. We will ask the patient to fill out two questionnaires. These may take 10 to 15 minutes to fill out. A brief battery of neuropsychiatric or memory tests will be administered at the months 6 and 12 study visits which can take about 45 minutes to complete. We would also like to collect a small sample of blood (less than two tablespoons) at each visit.

21 Day Visit

- Assessment Interview: You will be contacted by phone to schedule a 6 month follow up visit. If a member of the research staff is unable to contact you by phone, they will contact your next of kin, a certified letter will be sent to you.

6 Month Visit:

- Assessment Interview: You will be asked about your medical history, your smoking history, and your alcohol use, since the 21 day study visit. You will be asked to complete questionnaires about your quality of life. Also, a brief set of tests will be given to test your memory.
- Blood Samples: You will provide as much as 2 tablespoons of blood to be shipped to Fisher BioServices for storage and future use.

12 Month Visit

- Assessment Interview: You will be asked about your medical history, your smoking history, and your alcohol use, since the 6 month study visit. You will be asked to complete questionnaires about your quality of life. Also, a brief set of tests will be given to test your memory.
- Blood Samples: You will provide as much as 2 tablespoons of blood to be shipped to Fisher BioServices for storage and future use.

Acetaminophen Questionnaire

If your liver injury or liver failure was due to acetaminophen, the active ingredient in Tylenol ® and many over-the-counter pain relievers and medication, you will be asked to fill out a separate questionnaire during your recovery.

- A study coordinator will contact you and obtain consent prior to enrolling you in this part of the study.
- If you choose not to fill out the questionnaire, you may still participate in the other portions of this study. This questionnaire includes information regarding: prior awareness of acetaminophen toxicity, previous overdoses, depression and impulsivity data. Every intentional/suicidal acetaminophen overdose patient automatically receives a psychiatric consult as part of their standard of care and must be cleared for discharge by the psychiatric team. A psychiatric consult will also be made for any unintentional acetaminophen overdose patient who is found to be clinically depressed and/or suicidal.

Change of Diagnosis from ALI to ALF:

If you are being enrolled in this study with a current diagnosis of ALI (checked on page 1 of this consent form), you may become sicker over the course of your illness. If you become sleepy or confused in addition to your current symptoms, you may have progressed from acute liver injury to acute liver failure. Researchers would like to continue to follow you and obtain blood samples as outlined in this consent form.

Because your diagnosis may have changed, there will be an additional blood collection procedure for your participation in the acute liver failure study. At most, you will have two tablespoons of blood drawn each day for seven additional days with no more than 14 days of blood collection and a one-time collection of urine. Because you may not be thinking clearly, we will also discuss your continued participation with your legally authorized representative that you have chosen.

You will indicate “yes” or “no” at the end of this consent form and initial and date whether you consent to participate in the acute liver failure portion of the study should your diagnosis change from ALI to ALF.

How will my samples be identified?There are no experiments being conducted. The only research involved in this project is gathering additional blood and urine samples and tissue (if available) and clinical data from your hospital admission for future testing. All of the samples collected as part of this study will be shipped and stored in the National Institute of Diabetes, Digestive, and Kidney Disease (NIDDK) Central Repository for future research use.

<u>NIDDK Repository</u>
The NIDDK Central Repository is a research resource supported by the National Institutes of Health. The Repository collects, stores, and distributes biological samples and associated data from The purpose of this collection is to make samples available for use in research for the study of acute liver failure or injury after the current study is completed. Sending samples to the NIDDK Central Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent liver disease.

The NIDDK Central Repository will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before researchers in this study send samples to the Repository, each sample will be given a unique code number. Your name and all personal identifying information such as your address, social security number, and date of birth will be removed from the samples. The Repository will not be able to give out your name or other information that identifies you to the scientists that receive the samples. The Repository staff and scientists will have some data about you such as your age, sex, diagnosis, and race.

Since, in many instances, the cause of liver damage is not known, these samples will allow researchers to determine whether viruses or poisons of some kind have affected the liver leading to its injury to function.

Your samples may be used in other research studies only if the other research has been reviewed and approved by an Institutional Review Board (IRB). The IRB is a group of people who are responsible for assuring that the rights of participants in research are respected.

Donation and storage of blood sample(s) in the Repository is voluntary, and if you choose not to have your sample(s) stored in the Repository there will be no penalty or loss of benefits to which you are entitled. If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the study. When study researchers receive written instructions from you requesting that your stored sample(s) be destroyed, the Repository will destroy your sample(s). After the study ends, however, you will not be able to withdraw your sample because the Repository will not know which one is yours.

Your samples will stay in the NIDDK Central Repository indefinitely.

You will not receive any direct benefit or payment for agreeing to store your sample(s) in the Repository, but your sample may benefit the future health of the community or a particular group. Because other researchers will not have access to your identity, neither you nor your physician will get the eventual results of studies that might be performed using your sample(s). It is possible that data resulting from the use of your stored sample(s) may eventually be used in research publication(s). In that event, your name or other identifying information will not be included, as this information will not be available to the researchers.

You will indicate “yes” or “no” at the end of this consent form and initial and date whether you consent to store your samples for future research

How long can I expect to be in this study?

If you join this study, you have inpatient study visits and 3 follow up study visits. You will be asked to have a follow up visit 21 days after your hospital discharge and 6 and 12 months after your hospital discharge. You will be in this study for 12 months (1 year). Study visits will last 15 minutes to 1 hour.

What if you want to stop before your part in the study is complete?

You can choose to stop participating at any time, for any reason without any penalty. However, if you decide to stop participating in the study, we encourage you to tell the researchers.

What are the possible risks and discomforts of the study?

Participation in this study might involve the following risks and/or discomforts to you*:*

Questions of a Personal Nature

Some of the questions we will ask you as part of this study may be sensitive in nature

and make you feel uncomfortable. You may refuse to answer any or all of the questions, take a break or stop your participation in this study at any time.

Loss of Confidentiality
Any time information is collected there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks of Blood Drawing
Blood samples will only be obtained at scheduled blood drawings, so that no additional needle sticks will be involved. A small sample (two tablespoons) will be obtained daily for the first seven study days. This amount of blood is not considered to make a difference in a patient's condition, since even over the seven days it represents 1/25th of the total blood volume present. This amount can be restored by the bone marrow each day. With blood drawing, the patient may experience slight discomfort, bleeding, and/or bruising, or may feel dizzy or faint. An infection can develop if the site is not kept clean. Medical personnel will obtain the samples and watch closely to determine whether there are problems needing medical care.

Other Risks
There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

What if we learn of new risks in the study?
Study researchers will provide you with any new information gained during the course of the study that might affect your willingness to continue participation.

What are the possible benefits of this study?
There will be no direct benefit to you from participating in this study. However, the information gained from your participation may help researchers understand more of the nature of acute liver injury. The researchers cannot guarantee that your family member will benefit from participation in this research. We hope the information learned from this study will benefit others with acute liver injury in the future. Information gained from this research could lead to better standard of care treatment.

What options are available if I decide not to take part in this research study?
This is not a treatment study. You do not have to be part of it to get treatment for your condition.

Will it cost you anything to participate in the study?
There will be no cost to you for the tests done on your blood samples or any other study procedures.

Will I be paid if I take part in this research study?

Neither you nor your relative will be compensated for participation in this study. Costs related to research (i.e., additional visits, blood draw) will be covered by the study.

There are no funds available to pay for parking expenses, transportation to and from the research center, lost time away from work and other activities, lost wages, or child care expenses.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e. the follow up visits mentioned above).

However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility. You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas or Parkland Health & Hospital System.

You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

Your doctor may be a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

If I agree to take part in this research study, can I be removed from the study without my consent?

Yes. The researchers may decide to take you off this study if:

- The sponsor cancels the research.
- Your liver damage is found to be caused from a competing chronic liver disease

Will my information be kept confidential?

Information about you that is collected for this research study will remain confidential unless you give your permission to share it with others, or as described below. You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- National Institute of Health;
- National Institute of Diabetes and Digestive Kidney Disease;
- Fisher BioServices;
- Data Coordination Unit at Medical University of South Carolina
- Representatives of government agencies, like the US Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

To help us further protect the information the investigators has obtained a Certificate of Confidentiality from the U.S. Department of Health and Human Services (DHHS). This Certificate adds special protections for research information that identifies you and will help researchers protect your privacy.

With this Certificate of Confidentiality, the researchers cannot be forced to disclose information that may identify you in any judicial, administrative, legislative, or other proceeding, whether at the federal, state, or local level. There are situations, however, that legally require disclosure, such as:

- to DHHS for audit or program evaluation purposes;
- information regarding test results for certain communicable diseases to the Texas Department of State Health Services, including, but not limited to HIV, Hepatitis, Anthrax, and Smallpox;
- if you pose imminent physical harm to yourself or others;
- if you pose immediate mental or emotional injury to yourself;
- if the researchers learn that a child has been, or may be, abused or neglected; or
- if the researchers learn that an elderly or disabled person has been, or is being, abused, neglected or exploited.

The researchers will not, in any case, disclose information about you or your

participation in this study unless it is included in the Authorization for Use and Disclosure of Protected Health Information for Research Purposes as stated above.

The Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about your involvement in this research study. In addition, the researchers may not use the Certificate to withhold information about your participation in this research study if you have provided written consent to anyone allowing the researchers to release such information (including your employer or an insurance company). This means that you or your family must also actively protect your privacy.

A Certificate of Confidentiality does not represent an endorsement of this research project by the Department of Health & Human Services or any other Federal government agency.

Whom do I call if I have questions or problems?

For questions about the study, contact Dr. William Lee or his designee at 214-645-6111 during regular business hours and at 214-645-0595 after hours and on weekends and holidays.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

Optional Storage of Blood and Urine Samples	
Please indicate your response by initialing below:	
_____**YES**, I agree to have my blood and urine samples to be stored for future research (testing for viruses, poisons, and other causes of acute liver failure).	Initials/Date:
_____**NO**, I DO NOT agree to have my blood and urine samples to be stored for future research (testing for viruses, poisons, and other causes of acute liver failure).	Initials/Date:

Optional Storage of Tissue Samples

Please indicate your response by initialing below:	
_____**YES**, I agree to have my liver tissue samples stored for future research (testing for viruses and pathological changes of different causes of acute liver failure).	Initials/Date:
_____**NO**, I DO NOT agree to have my liver tissue samples stored for future research (testing for viruses and pathological changes of different causes of acute liver failure).	Initials/Date:

Optional Diagnosis Change from ALI to ALF Please indicate your response by initialing below:	
_____***YES**, I agree to have the extra blood draws done should my diagnosis change from ALI to ALF.*	Initials/Date:
_____ **NO, I DO NOT** *agree to have the extra blood draws done should my diagnosis change from ALI to ALF.*	Initials/Date:

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.
- You understand that a copy of this signed consent document, information about this study and the results of any test or procedure done may be included in your medical record and this information may be available to health care providers and authorized persons including your insurance company.

_____

Name of Participant (Printed)

_____ _____ _____ AM / PM

Signature of Participant Date Time

_____

Legally Authorized Representative's Name (Printed)

_____ _____ _____ AM / PM

Legally Authorized Representative's Signature Date Time

_____

Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time

Interpreter Statement:

I have interpreted this consent form into a language understandable to the participant and the participant has agreed to participate as indicated by their signature on the associated short form.

_____

Name of Interpreter (Printed)

_____ _____ _____ AM / PM

Signature of Interpreter Date Time