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RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

TITLE: Observational Study of Hepatitis B Virus (HBV) in Patients Coinfected with Human Immunodeficiency Virus (HIV)

VCU IRB PROTOCOL NUMBER: HM20000444

INVESTIGATOR: **Richard K. Sterling, MD, MSc**
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(804) 828-4060 (24 hours)

SPONSOR: NIH-NIDDK

If any information contained in this consent form is not clear, please ask the study doctor or the study staff to explain any information that you do not fully understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

PURPOSE OF THE STUDY

Infection with both Hepatitis B Virus (HBV) and Human Immunodeficiency Virus (HIV) also known as coinfection is common in those living with human immunodeficiency virus (HIV). You are currently being treated for your HIV. Because there may have been a period of time when your HBV was not controlled, there is the chance that liver injury could have occurred. The purpose of this study is to define the degree of liver injury in patients with HIV-HBV coinfection, examine the role HIV treatment may have on the suppression of HBV, and to establish non-invasive ways to assess liver damage, as well as monitoring for long-term complications of HBV treatment as part of your HIV regime.

DESCRIPTION OF THE STUDY

In order to be eligible for this study, you must be coinfected with both HIV and HBV and currently receiving treatment for your HIV. Although the effects of your current HIV treatment on your HBV virus will be studied, this is not a direct treatment study since you are already receiving treatment for your HIV.

Your participation in this study will last up to four years. Approximately 250 individuals will participate in this study at a total of eight (8) clinical sites throughout the United States.

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The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the National Institutes of Health (NIH) is providing the funding for this study.

PROCEDURES

If you decide to be in this research study, you will be asked to sign this consent form after you have had all your questions answered.

At your first study visit (Visit 1), if you agree to participate, you will be asked to sign this informed consent statement. Your medical history will be taken and a physical exam will be performed. This exam will include measurements of your height, weight, waist measurement, and vital signs (pulse, blood pressure and temperature). Information such as age, gender, race, ethnicity, duration of infections, how you may have acquired the infections, and current and past treatments for both HIV and HBV will be recorded. Blood and urine samples, as part of routine assessment for both HIV and HBV, will be obtained. These tests and information are routine and not unique to the study.

Blood samples, specific to the study and not considered to be routine standard of care will also be collected for determination of bone health, and to examine glucose and insulin metabolism. In addition, blood collection for specialized HBV virus testing and a test assessing the degree of liver inflammation will be collected. You will not be charged for these blood specimens that are considered unique to the study. Up to 7 tablespoons (105 ml) of blood will be collected.

You will also be asked to complete questionnaires; these are to assess past or current alcohol use and current symptoms that might be associated with liver disease.

If you have had a liver biopsy within the past 3 years we will obtain biopsy slides and collect information from the pathology report. If you have not had a liver biopsy within 3 years, you will be asked to undergo a *baseline* liver biopsy to assess the severity of your disease. This baseline liver biopsy is important to assess whether you have developed any significant liver disease during the time in which you had hepatitis B and did not receive treatment or the treatment was not completely effective. You will be asked to sign a separate consent for this procedure.

Specimen Banking and Data Repository:
Blood samples will first be collected and stored at VCU Medical Center and the study's Central Laboratory. Blood samples will also be sent to, and stored at, the NIDDK Central Repository. These samples may be used for future testing.

The Central Laboratory and NIDDK Repository will take measures to protect your privacy, but no guarantee can be absolute. At the Central Laboratory and NIDDK Repository, your blood samples will be identified only by a code, and neither will have access to your name or other identifying information. Certain clinical information about you will also be stored at the Central Laboratory and NIDDK Repository to help investigators interpret the results of tests done on the blood. You will not see any of the

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results from tests performed for research purposes. There is no cost to you or your insurance company for storing and testing the specimens for research purposes.

Liver biopsy samples will first be collected and stored at the VCU Medical Center. Liver biopsy samples will also be sent to, and stored at, the NIDDK Central Repository. Samples which will be read by study pathologists for research purposes will be identified only by a code. Certain clinical information about you will be used to interpret the results of these tests. You will not see any of the results from tests performed for research purposes. These samples may be used for future research.

The NIDDK Central Repository is a research resource supported by the National Institutes of Health. The Central Repository collects, stores, and distributes biological samples and data from many studies, including this one. The purpose of a Central Repository is to make samples and information available for research after this study is completed. Sending samples to the Central Repository may give scientists valuable research material. This material may help scientists develop new medical tests, treatments, and ways to prevent diseases.

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. The sample will stay in the 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.

There is a small chance that research using your stored sample(s) may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people.

Research using your stored sample(s) may lead to findings or inventions that may have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. There are no plans to offer you compensation for any present or future products, processes, and /or therapies developed as a result of research using your stored sample(s).

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Follow up visits: Once you are enrolled in the study, you will be asked to participate for four (4) years or until the study ends, whichever comes first. You will be asked to return for a follow-up visit to the clinic every six (6) months, for up to 48 months (or sooner if clinically indicated). This will part of your routine care to monitor your liver disease. At these follow-up visits, you will be asked to provide blood. The amount will be between 30 ml (about 2 tablespoons) and 105 ml (about 7 tablespoons), depending on the visit. Some of this blood may be used for routine care, and some for research testing unique to the study, as described above.

Participants who have been enrolled in the study for three or more years will be asked to have the liver biopsy repeated at the completion of the study; this repeat, end of study liver biopsy will be paid for by the study. The purpose of this second liver biopsy to determine if your liver disease has worsened or improved over time.

RISKS AND DISCOMFORTS

Physical harm associated with participating in this study is limited. In this study we are asking to collect blood samples. Drawing blood can cause temporary discomfort or bruising at the skin puncture site and in rare instances (less than 1%), fainting or an infection can occur. Precautions will be taken to avoid these difficulties.

Of minimal risk to you is the possible inconvenience of taking the time to report your medical status to the research coordinator or to complete a questionnaire.

Liver biopsy: A liver biopsy is a standard procedure used by liver specialists to assess the health of your liver. The procedure includes numbing the skin over the liver with a local anesthetic, followed by passing a needle through the skin into the liver and removing a small core of liver tissue. A specialist will examine the tissue carefully under the microscope. There may be some discomfort associated with the procedure. The discomfort should generally not last more than several hours. The risks include bleeding from the biopsy site, significant bleeding requiring a blood transfusion or surgery to control the bleeding (less than 1/1,000 patients), perforation of internal organs (less than 1/1,000 patients) and death (less than 1/10,000 patients). You will be asked to sign a separate consent form for this procedure.

GENETIC TESTING

The purpose of this research study is to collect and store blood samples for future analysis and genetic research studies related to Hepatitis B. The purpose of this consent form is to give you information so that you can decide whether you want to provide an additional blood sample.

Techniques have been developed that allow studying inherited factors called genes and the genetic make-up of your cells, called DNA. By studying material (DNA and RNA) obtained from your blood sample, researchers might identify gene(s) that carry the trait(s) for Hepatitis B diseases and its risk factors. RNA assists in transmitting genetic

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information from DNA. DNA can be examined directly or some of the blood cells can be made into a "cell line" that can be grown indefinitely in a laboratory (serving as a "bank" for your genes). A cell line gives researchers an unlimited supply of DNA that can be used for future genetic studies without having to draw more blood from you.

If you agree to participate, study personnel will draw a blood sample of approximately 1-2 tablespoons. Whenever possible, blood for the genetic research discussed above will be drawn at the same time as samples for other required laboratory tests. If not, an additional needle stick might be required. It may be necessary to redraw this sample if for some reason the first sample is unusable.

Participation in this genetic research study is entirely voluntary. If you decide that you do not want to participate in this genetic research study, you may still continue to participate in the study. Approximately 250 subjects will be asked to participate in this genetic bank research study.

Genetic research is an important way for researchers to learn about the role of genes in health and disease. Genetic research is often done to discover genes, find out how genes work, or help researchers learn how to use what we know about genes to treat or prevent disease.

The investigators associated with this research study and possibly researchers not involved with this research study may be given access to your blood samples or cell lines. If a portion of your blood sample or cell line is sent to other researchers, only a code number will be sent with your sample. No personal information identifying you will be sent or provided. The samples will be given to the researchers in such a manner that they will not be able to connect your identity with the sample or medical information. Information about you such as your race, ethnicity, sex or medical history may be made available to the investigators studying your blood. Such information might be important for research. Although no one can absolutely guarantee confidentiality, using a code number greatly reduces the chance that someone will ever be able to link your name to your sample or to your results.

Any information about you obtained from this research will be kept as confidential (private) as possible. You will not be identified by name in any publication of research results unless you sign a separate form giving your permission (release). It is possible that authorized representatives of the Food and Drug Administration, or the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which funds this study, or the University of Pittsburgh Data Coordinating Center may inspect your research records. The fact that you are participating in a research study and that you are undergoing certain research procedures (but not the results of the procedures) may also be made known to individuals involved in insurance billing and/or other administrative activities associated with the conduct of the study. Information resulting from the research will not be entered into your medical records.

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There are several things you should know before allowing your DNA to be studied or stored for future study:

- This research will use blood samples. The blood samples will be stored indefinitely or until the cells or genetic material (DNA) used for testing are no longer viable (living). You can request to have your samples destroyed at any time.
- Personal genetic information discovered through the study will not be provided to you. This research will not have an effect on your care; therefore, you, your family, or your doctor will not receive results of these studies, and the results will not become a part of your medical record.
- The use of your biological sample will be under the guidance of the Principal Investigators of this research project. To protect your confidentiality, your biologic samples and genetic material will be assigned a code number. The stored samples will not contain personal identifiers. The records linking your personal identity to the blood samples to the code number will be stored in locked research files at VCU Medical Center.
- Your blood sample (DNA) will be sent to the NIDDK Central Repositories, a research resource supported by the National Institutes of Health. The Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research for the study of hepatitis B and related conditions. Sending samples to the Repository may give scientists valuable research material that can help them develop new diagnostic tests, new treatments, and new ways to prevent diseases.
- There will be no direct benefit to you as a result of the genetic research performed with the material obtained from your blood sample. A possible indirect benefit is that your participation might contribute to the knowledge about Hepatitis B, or might help in developing early diagnosis methods or new treatments.
- You have been informed previously that the personal results of the genetic research as described above will not be given to you. You or your representative will be notified promptly if any other information develops during the course of the study that might cause you to change your mind about continuing to participate.
- There will be no cost to you for participation in this genetic research study. You or your insurance carrier will not be billed either for the preparation of your biologic samples and genetic material or for the shipping and handling of these samples.
- You will not be paid for participation in this genetic research study. Your biologic samples and genetic material might lead, in the future, to new inventions or products. If the research investigators are able to develop new products from the use of your biologic sample or genetic material, there are currently no plans to share with you any money or other rewards that may result from the development of the new product.
- If you should decide to withdraw your consent for the use of your biologic samples or genetic material, please give this request in writing to the study doctor

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listed on the front page of this consent form. Upon receipt of this request, your biologic samples, genetic material, and related personal information will be destroyed. 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. The sample will stay in the Repository indefinitely. Withdrawal from the genetic study will not affect your participation in this study.

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

Authority to Request Protected Health Information

The following people and/or groups may request my Protected Health Information:

- Principal Investigator and Research Staff
- Research Collaborators
- Data Safety Monitoring Boards
- Others as Required by Law
- Study Sponsor
- Institutional Review Boards
- Government/Health Agencies

Authority to Release Protected Health Information

The VCU Medical Center may release the information identified in this authorization from my medical records and provide this information to:

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

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

Type of Information that may be Released

The following types of information may be used for the conduct of this research:

X Complete health record	X Diagnosis & treatment codes	X Discharge summary
X History and physical exam	X Consultation reports	X Progress notes
X Laboratory test results	X X-ray reports	X X-ray films / images
☐ Photographs, videotapes	☐ Complete billing record	☐ Itemized bill
X Information about drug or alcohol abuse		X Information about Hepatitis B or C tests
X Information about psychiatric care		X Information about sexually transmitted diseases

X Other (specify): Patient codes

Right to Revoke Authorization and Re-disclosure

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You may change your mind and revoke (take back) the right to use your protected health information at any time. 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.

BENEFITS TO YOU AND OTHERS

This is not a treatment study, and you are not expected to receive any direct medical benefits from your participation in the study. The information from this research study may lead to a better treatment in the future for people with HIV-HBV coinfection. You may benefit from the physical exams, lab tests, and other study procedures.

COSTS

It will not cost you anything to participate in this study. If you enroll in this study, you will have some tests and procedures done that are part of the research but may overlap with your regular medical care. Neither you, nor your insurance provider, will be charged for the costs of any of the research procedures for the purpose of this study (i.e., the screening procedures, experimental procedures, or monitoring/follow-up procedures described above).

Clinical evaluation, blood tests and procedures including the *baseline* liver biopsy, performed as part of standard of care for monitoring your hepatitis B, will be charged to you or your insurance. The liver biopsy performed at year four (4) will be paid by the study.

PAYMENT FOR PARTICIPATION

You will not be paid for your participation in this study. We will not pay for your medical care as part of this study.

ALTERNATIVE

If you decide not to enter this study, your alternative is not to participate in this study.

CONFIDENTIALITY

Your participation in this study will be kept confidential. No one other than study personnel at the clinic will be given your name, address, and other personal identifying information. The information obtained for this study will be labeled with only an identifying number and code. No one outside the clinical center where you complete visits can link your name or other personal identifiers to this code. Using this code, your research information will be sent to the Data Coordinating Center located at the University of Pittsburgh, Graduate School of Public Health in Pittsburgh, Pennsylvania.

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As this is a multi-center federally funded study, the anonymous study data for all study participants may be made available to aid other researchers. When results from this study are published, you will not be identified by name.

Representatives of the National Institutes of Health and the Data Coordinating Center, or other experts, may review your records at visits to the clinic. This is part of the ongoing monitoring of the study. In addition, representatives from the United States Food and Drug Administration (FDA) or the Institutional Review Board at this institution may review your study records, including your medical records. To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. This will allow us to resist any demands for your health information, with a few exceptions as explained below.

The Certificate of Confidentiality protects the study from being forced to disclose information that may identify you, even from a court subpoena. It is also protected from requests for your information made by federal, state, local civil, criminal, administrative, legislative, or other entities. However, the Certificate cannot be used to resist a demand from the U.S. Government used to audit or evaluate federally funded projects. Nor does it protect information that must be disclosed in order to meet the requirements of the U.S. Food and Drug Administration. The Certificate does not prevent you or a member of your family from voluntarily releasing information about you or your involvement in the research. If an insurer, employer, or other person obtains your written consent to receive research information, then we may not use the Certificate to withhold that information. Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse or neglect, or a risk of harm to yourself or others, we are required to notify the proper authorities.

You should know that research data or (medical information if applicable) about you may be reviewed or copied by the sponsor of the research or by the Virginia Commonwealth University. Authorized representatives of the VCU Research Conduct and Compliance Office may review your information to monitor the appropriate conduct of this research study.

All records related to your involvement in this research study will be stored in a locked file cabinet. In this study, you will be given a unique study identification number, which will be written on your study forms. However, your name will appear on some study-related forms such as this consent form and private study information records. Your name, study identification number, this consent form and any information that could identify you will be kept separate from the research records. During quality assurance visits, the study's sponsor (NIDDK) or designee, or the Institutional Review Board may wish to review your medical record. One of the investigators will supervise the representatives from these agencies, who will not record your name.

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.

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At most, the Website will include a summary of the results. You can search this Web site at any time.

COMPENSATION FOR INJURY or ILLNESS

Virginia Commonwealth University and the VCU Health System have no plan for providing long-term care or compensation in the event that you suffer injury as a result of your participation in this research study.

If you are injured by, or become ill, from participating in this study, please contact your study doctor immediately. Your study doctor will arrange for short-term emergency care 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.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is voluntary. You may decide to not participate in this study. If you decide not to be in this study or decide to stop participating in this study after enrolling, it will not affect your medical care in any way. Your decision to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

You have the right to change your mind about allowing us to have access to your personal health information. You may also tell us that you no longer allow us to use or disclose your de-identified information for this study. If you choose to take away this permission you must inform Dr. Sterling in writing. Deciding to remove your information from the study will not result in any penalty or loss of benefits to you.

You may revoke (choose to withdraw) this Authorization as provided under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) at any time after you have signed it by providing the study staff at VCU Medical Center with a written statement that you wish to withdraw this Authorization. Your withdrawal of this Authorization will be effective immediately. Your Protected Health Information would no longer be used/disclosed for research purposes by VCU Medical Center and the other persons or entities that are identified in the "Confidentiality of Records" section of this consent. The exception is the extent to which VCU Medical Center or the other persons or entities identified above have already taken action based on your consent. In addition, your Protected Health Information may continue to be used or disclosed to preserve the integrity of an ongoing study.

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Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent. The reasons might include:

- the study doctor thinks it necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study; or
- administrative reasons require your withdrawal.

QUESTIONS

In the future, you may have questions about your study participation. If you have any questions, complaints, or concerns about the research, contact:

Dr. Richard Sterling
VCU Medical Center
1200 E. Broad Street
Richmond, VA 23298
(804) 828-4060 (24 hours), pager #(804) 828-0951

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

Office of Research
Virginia Commonwealth University
800 East Leigh Street, Suite 113
PO Box 980568
Richmond, VA 23298
(504) 827-2157

Contact this number for general questions, 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.

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.

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 once I have agreed to participate.

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Consent for Genetic Testing:

Please initial one of the following:

_____ I give permission for my blood samples to be used for genetic testing. Specimens may be stored for as long as they can be used. Specimens can be used for genetic research that is not yet planned and may be performed after the completion of the Hepatitis B Research Network Cohort Study.

_____ I **do not** give permission for my blood samples to be collected or stored for genetic research.

_____
Participant Name, printed

_____ _____
Participant Signature Date

_____
Name of Person Conducting Informed Consent Discussion
(Printed)

_____ _____
Signature of Person Conducting Informed Consent Discussion Date

_____ _____
Principal Investigator Signature (if different from above) Date

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