UNIVERSITY OF CALGARY

TITLE: A Prospective Study of Hepatitis B Virus (HBV) Immunity and Hepatitis B Vaccination in Patients with Non Alcoholic Fatty Liver Disease (NAFLD) in Canada

SPONSOR: Canadian Institutes of Health Research / GlaxoSmithKline

INVESTIGATORS: Dr. Carla Coffin and Dr. Craig Jenne

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

BACKGROUND

The hepatitis B virus (HBV) is a global human pathogen that affects at least 2 billion people worldwide including ~240 million chronic hepatitis B (CHB) carriers that are at risk for end-stage liver disease. Although current guidelines recommend that certain high-risk populations receive hepatitis B immunization, appropriate identification and compliance is generally much lower in adults compared to children.

According to the most recent Canadian Association for the Study of Liver Disease guidelines, all adults with diabetes, as well as all patients with chronic liver disease should receive the hepatitis B vaccine. The basis for these recommendations are two-fold, (1) diabetics may be at risk of blood-borne virus (BBV) exposure through contact with contaminated blood glucose monitoring devices and (2) diabetic patients are at increased risk of the metabolic syndrome and the development of non-alcoholic fatty liver disease (NAFLD). Therefore the main incentive for HBV vaccination in diabetics is due to the concomitant risk of the metabolic syndrome and advanced liver disease due to NAFLD. We propose that adults with NAFLD should undergo comprehensive screening for hepatitis B immunogenicity, in addition to screening for infection, and catch up or booster vaccinations should be administered to non-immunized patients with confirmatory immunity testing thereafter.

WHAT IS THE PURPOSE OF THE STUDY?

Due to missed childhood vaccination programs, the majority of adult patients with NAFLD in Canada do not have immunity to hepatitis B. Adults with NAFLD who receive the HBV vaccine have reduced immune responses in the setting of obesity. We would like to determine immunity against hepatitis B in a sample of adult NAFLD patients. We would also like to determine HBV vaccine responses (anti-HBs titres, HBV specific B and T cell responses) in adult NAFLD patients.

WHAT WOULD I HAVE TO DO?

You have been chosen to take part in this research because you have been diagnosed with Non Alcoholic Fatty Liver Disease (NAFLD) or Non Alcoholic Steatohepatitis (NASH) and have been referred to the NAFLD clinic.

To participate in this research, we are asking you for your permission to obtain and record your health data in a de-identified manner, to agree to be contacted by the researchers, and to allow us to collect extra blood at the time you are getting a standard of care blood draw, by signing this consent form. Your records will be obtained from your clinic chart, as well as online clinical records (Sunrise Clinical Manager, Alberta Netcare, Etc.). All other procedures are normally done as standard of care in the NAFLD clinic.

Regular procedures that normally occur in the clinic include:

- Initial clinical investigations (i.e., labwork and Fibroscan) to determine if you will be triaged as low, moderate, or high risk.
    - Low risk patients are those who do not have any risk factors for progression to cirrhosis, or development of NAFLD complications.
    - Moderate risk patients who have risk factors for progression to fibrosis, or who already have fibrosis are seen in clinic by a hepatologist.
    - Finally, high risk patients include those with metabolic syndrome, poorly controlled diabetes or hyperlipidemia that is difficult to treat.
- Blood tests for Hepatitis B (HBV) will be done to determine if you are immune to HBV (by natural exposure or immunization). If you are not immune to HBV, you will be offered a vaccination of the virus that will include 3 different doses (baseline, 1 month and 6 month injections). This vaccination will not cost you anything, as it will be covered under your healthcare plan.
- A blood test will be taken at baseline and one month after your last dose of the vaccine to determine your immunity to HBV. If your healthcare plan only covers a portion of the vaccine, the researchers will reimburse you for your costs.
- During your blood tests, the researchers will obtain extra blood for research purposes (approximately 40-50 ml which is equal to 10 tablespoons).

WHAT ARE THE RISKS?

The risks of participating in this study are the same as if you did not participate. All procedures are being done as standard of care. The only risk that may occur could be pain or bruising around the puncture site for the blood draw and vaccination.

WILL I BENEFIT IF I TAKE PART?

If you agree to participate in this study there may or may not be a direct benefit to you. The information we get from this study may help us to understand hepatitis B vaccine responses in future for patients with NAFLD or NASH.

DO I HAVE TO PARTICIPATE?

This study is voluntary and you may withdraw from the study at any time without jeopardizing their health care by contacting the researchers to let them know you would like to withdraw. Any information that has already been collected up to the time you take back your permission will have been entered into a database that has no personal identifiers associated with you. This data cannot be retrieved and will therefore be kept.

If new information becomes available that might affect your willingness to participate in the study, you will be informed as soon as possible.

WILL I BE PAID FOR PARTICIPATING, OR DO I HAVE TO PAY FOR ANYTHING?

You will not be paid for participating in this study. If your healthcare plan only covers a portion of the vaccine, the researchers will reimburse you for your costs.

WILL MY RECORDS BE KEPT PRIVATE?

Only the researchers will have access to your identifiable health records (clinic charts and online health records from various sources such as Alberta Netcare, Sunrise Clinical Manager, etc.) which will be protected by the researchers by being locked in the secure research office and recorded on an encrypted database. No identifiable data will leave the research site. You will be assigned a unique ID so no identifiers will be recorded. Your information will be de-identified and lumped together with all other participant data when conducting the statistical analyses. The Conjoint Health Research Ethics board will also have access to the research files in order to ensure all research is being conducted in an ethical manner.

IF I SUFFER A RESEARCH-RELATED INJURY, WILL I BE COMPENSATED?

In the event that you suffer injury as a result of participating in this research, no compensation will be provided to you by Canadian Institutes of Health Research, GlaxoSmithKline (GSK), the University of Calgary, Alberta Health Services or the Researchers. You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

SIGNATURES

Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a participant. In no way does this waive your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time without jeopardizing your health care. If you have further questions concerning matters related to this research, please contact:

Sarah Haylock-Jacobs (403) 220-7808

Dr. Coffin (403) 592-5049

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

Participant's Name	Signature and Date
Investigator/Delegate's Name	Signature and Date
Witness' Name	Signature and Date

The University of Calgary Conjoint Health Research Ethics Board has approved this research study.

A signed copy of this consent form has been given to you to keep for your records and reference.