Department of Veterans Affairs	VA RESEARCH CONSENT FORM Version Date: *12/27/2018*		
Title of Study: **ID#**:	**Metabolic Effects of Natriuretic Peptide Hormones**		
Principal Investigator:	**Katherine N. Bachmann, M.D.**	**VAMC: (626)**	Tennessee Valley Healthcare System (VA TVHS)
Participant Name:		**Date:**	

PURPOSE OF THE STUDY

You are being asked to take part in a research study at the VA Tennessee Valley Healthcare System Medical Center because you are a healthy volunteer without significant medical problems, and you have a body mass index (BMI) either in the normal range (18.5-25 kg/m^2) or in the obese range (greater than 30 kg/m^2). We intend to recruit a total of 50 subjects for this study (25 lean and 25 obese). This study is sponsored by the VA.

The purpose of this study is to learn about the effects of natriuretic peptide hormones on metabolism, specifically on energy and fat metabolism.

Natriuretic peptides (NPs) are hormones produced by the heart to maintain its structure and function. NPs are well-known for their important role in blood pressure regulation. In addition, in recent years, findings from scientific studies suggest that the NPs may also have effects on metabolism. Studies in animals have suggested that natriuretic peptide hormones may protect against fat accumulation, and may affect energy and fat metabolism. However, much more information must be learned about the effects of natriuretic peptide hormones on energy and fat metabolism in humans.

In this study, we will study the effects of recombinant human b-type natriuretic peptide hormone (BNP (1-32)) on metabolism, specifically on energy and fat metabolism. The goal of this study is to provide important information about the role of the NP system on metabolism in humans.

The study will consist of 3 visits: Screening Visit, Study Visit 1, and Study Visit 2.

- Screening Visit: Approximately 60 minutes duration
- Study Visit 1: (Approximately 0.5-2 weeks after Screening Visit); Approximately 7 hour duration
- Study Visit 2: (At least two weeks after Study Visit 1); Approximately 6 hour duration

DESCRIPTION OF THE PROCEDURES AND APPROXIMATE DURATION OF THE STUDY

If you agree to participate in this research study, it will take you approximately 1-2 months to complete the study. During this time we will ask you to come in for a screening visit to determine eligibility. If eligible, you will complete two additional visits. There will be at least two weeks in between the 2 main study visits.

Research investigational procedures being performed at Vanderbilt University Medical Center (VUMC):

Some or all aspects of the screening visit (as detailed below) may occur at Vanderbilt University Medical Center (VUMC). If you are deemed eligible for the study, the subsequent main study visits (Study Visits 1 and 2) will occur at the VUMC Clinical Research Center (CRC), located at the Vanderbilt University Medical Center main campus. Details for each study visit are outlined below. Also, VUMC is permitting access to your medical records to the research study team. This will allow the study team to have access to information that may be relevant to your study participation.

Screening Visit

This visit will be approximately 60 minutes in length. During this visit, we will tell you about the study and review the consent form in detail, have you sign the consent form, and perform tests and procedures to see if you qualify to take part in this research study. The study doctor will review the results of these tests. If you do not qualify, the study staff will tell you why.

At this visit, we will:

- Ask about your medical history.
- Give you a physical exam, including measurement of height, weight and vital signs (e.g. blood pressure and heart rate).
- Test your blood or urine for pregnancy if you are a woman able to become pregnant. (Women who are pregnant or breastfeeding cannot take part in this research study).
- Collect a blood draw of about 7.5 ml (1/2 tbsp) to check your thyroid function, blood counts, electrolyte and fluid balance, kidney function, liver function, and glucose levels.

Whenever possible, we will combine the research screening tasks and procedures with standard-of-care tasks and procedures that you receive from your usual clinical providers. If the study team can determine your eligibility based on your information gathered from your standard-of-care tasks and procedures, you may not need to come in for a specific screening visit. This will be at the discretion of the study team.

Study Visits 1 and 2

We will ask you to collect your urine for 24 hours before your study visits. You will need to bring the urine collection with you to your visits.

During each of the two study visits, you will receive an intravenous (IV) infusion. During one visit, you will receive the infusion of BNP. During the other visit, you will receive an infusion of saline (salt water). Which infusion you receive at which visit will be determined randomly. Using a procedure like the flip of a coin, you will have a one in two chance of receiving the

BNP infusion at the first visit and the saline infusion at the second visit, and a one in two chance of receiving the saline infusion at the first visit and the BNP infusion at the second visit.

For each of these two visits, you will arrive fasting. This means that you cannot eat or drink anything (other than water) for at least 8 hours before your visit. Each visit will take approximately 6-7 hours to complete. Upon your arrival to the research facility, two peripheral intravenous (IV) lines, a blood pressure cuff on your arm and/or finger, and chest leads to monitor your heart will be placed. You will then be asked to lay supine (flat on your back) for the remainder of the study visit with breaks for urine specimen collection timepoints. While you are still supine, a non-restrictive clear hood will be placed over your head that has a tube which allows air (oxygen) in and air (carbon dioxide) out. The use of this machine (called a metabolic cart) will allow us to measure your resting energy expenditure. You will wear this hood for 30 minutes. Afterwards, we will begin the infusion of either BNP or saline. Blood will be drawn from an IV every hour starting right before the infusion begins. Energy expenditure will be measured 3 additional times during the day (for 30 minutes each time). At each study visit you will receive a total of 5 blood draws and 4 energy expenditure measurements. A total of approximately 140 ml (~9.5 tbsp) of blood will be drawn during each study visit. You will receive some fluids for hydration during the visit. Also, we will collect all your urine during your visits. Because body positioning is crucial for stable and reliable evaluation of our hormone measurements, you will need to remain supine (flat on your back) during the entire visit, except while urinating. Thus, while urinating, you will be instructed to use a bedside commode with the assistance of medical personnel. We will also monitor your blood pressure and heart rate throughout the infusions.

At the end of the infusion, you will undergo a biopsy of your subcutaneous fat tissue (under-the-skin fat tissue) on your abdomen, a few centimeters away from your belly button. This procedure will be performed by a trained study physician using sterile technique. A local anesthetic (lidocaine) will be used to numb the site of biopsy. A small incision (approximately 0.5 cm (1/5 inch)) will be made. Then a small liposuction cannula, with a syringe attached, is inserted and moved parallel to the skin until a small sample of tissue (less than the weight of a dime) is collected. After the biopsy is complete, antibiotic ointment will be applied followed by a steri-strip and adhesive bandage.

You will receive a Dual Energy X-Ray Absorptiometry (DXA) scan during the study. A DXA scan uses x-ray technology to measure bone thickness. During this test, X-ray pictures of your body will assess the amount of bone, fat, and muscle in your body. You will lie flat on a table and a machine will take pictures of different areas of your body. This test will last about 15 minutes.

Research procedures being performed at VA TVHS:

Some or all aspects of the screening visit (as detailed above) may occur at the VA depending on scheduling and availability. Also, the VA is permitting access to your medical records to the research study team. This will allow the study team to have access to information that may be relevant to your study participation.

Table Of Events:

Procedure	Screening Visit	Study Visit 1	Study Visit 2
Informed Consent	X		
Medical History & Physical exam	X		
Vital Signs, height, weight	X	X	X
Pregnancy test	X	X	X
Clinical Laboratory sample collection	X	X	X
24 hr urine collection		X	X
IV Infusion (Saline or BNP)		X	X
DXA scan		X	
Metabolic Cart		X	X
Fat Biopsy		X	X
Blood pressure, heart rate, and temperature monitoring		X	X

The table above and the description of study procedures above reflect the intended schedule of events. However, due to scheduling and logistical issues, there may be minor differences in the occurrence/sequence of events.

DESCRIPTION OF STUDY RELATED COSTS

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research.

However, you are still responsible for paying for the usual care you would normally receive for the treatment of any illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

PAYMENT FOR PARTICIPATION

You will receive compensation to help cover the cost of time and inconvenience. The amount that you are reimbursed is commensurate with the time and inconvenience incurred that you otherwise would not have incurred. You will receive $100 for completing Visit 1, and you will receive $400 for completing Visit 2, for a total of $500 for completing the entire study. You will receive the payment in the mail after you have completed your participation in the study. We ask that you join the study only if you intend on completing all study visits, as we need complete information in order to address the scientific question. You must agree to the release of personally identifying information such as your name, address and social security number to the VA Tennessee Valley Healthcare System so that you may receive your money. Your payment will be issued from the Austin Financial Service Center which will generate the IRS Form 1099 regardless of the amount of your participation compensation.

MEDICAL TREATMENT FOR RESEARCH-RELATED INJURY

Every reasonable safety measure will be used to protect your well-being. The VA has the authority to provide medical treatment to participants injured by participation in a VA project. VA medical facilities will provide necessary medical treatment to you as a research participant if you are injured as a result of your participation in this study.

Compensation may or may not be available to you under applicable state and federal law in the event that you suffer physical injury or illness arising from this study. By agreeing to participate in this study you are not waiving or giving up your legal rights to seek compensation. If you have questions you may contact the VA TVHS Institutional Review Board office at 615-873-6076 or the Research and Development Service office at 615-873-8694.

COMPENSATION FOR RESEARCH-RELATED INJURY

If you want to make a legal claim against the VA or anyone who works for the VA, special laws may apply. The Federal Tort Claims Act (28 U.S.C. 1346(b), 2671-2680) is a federal law that controls when and how a person can bring a claim against the U.S. Government. If you sign this document you are not giving up your right to make a legal claim against the United States.

If it is determined by the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at the Nashville VA to treat the injury, if you have VA benefits.

If you do not have VA benefits, if it is determined by the investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at Vanderbilt

Medical Center to treat the injury**.** There are no plans for Vanderbilt to pay for the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

DESCRIPTION OF THE DISCOMFORTS, INCONVENIENCES, AND/OR RISKS

Fasting: Inconvenience and low fluid status in the body. To minimize this risk, please drink plenty of fluids the day before the visits. Also, there is a potential risk of hypoglycemia (low blood sugar) while fasting. However, the risk of hypoglycemia in healthy individuals while fasting for this amount of time is low. Signs of hypoglycemia include dizziness, lightheadedness, extreme sweating, and extreme hunger; please let us know if you experience any of these symptoms.

Intravenous Lines: Risks related to the placement of peripheral intravenous lines are minimal. Risks include pain, hematoma formation, bruising, inflammation, and rarely fainting and infection.

Phlebotomy: The risks associated with phlebotomy in healthy individuals are minimal. Risks include pain, bruising, inflammation, and rarely fainting and infection. Other possible risks include low fluid status in the body and anemia (low blood counts).

Hemodynamic monitoring (blood pressure monitoring using sphygmomanometer and/or finger photoplethysmography, and heart rate monitoring by cardiac telemetry): A non-invasive technique with no symptoms aside from minimal discomfort.

BNP(1-32) (nesiritide): The main potential side effect of nesiritide is hypotension (low blood pressure). However, in healthy controls, BNP administered at doses and durations similar to what we will administer has been shown to be safe and well-tolerated, without significant hypotension or other significant adverse events. Other symptoms reported by subjects with heart failure who received nesiritide in prior trials include headache (8%), nausea (4%), and angina. Low blood pressure is extremely unlikely in this study, because your blood pressure will be closely monitored by trained medical personnel, and if your systolic blood pressure drops by ≥ 30 mmHg or your systolic blood pressure goes below 80 mmHg or you have symptoms due to low blood pressure as clinically assessed by trained medical personnel, the BNP infusion will be stopped. Because BNP is cleared quickly from the body, any blood pressure changes due to BNP would go away quickly after stopping the infusion. Finally, as with any drug, there is risk of allergic reaction; you will be closely monitored during the infusions, but please let us know if you develop any signs or symptoms of allergic reaction (like shortness of breath, swelling, or rash).

Subcutaneous adipose tissue biopsy: Possible risks of the biopsy procedure include pain, local skin irritation, bleeding, bruising, and hematoma at the site. There is potential risk for local or systemic infection, more severe bleeding, or a small scar; however, the risk of these events is extremely low.

Lidocaine: May cause local discomfort during injection, or a rash, redness or soreness at the injection site. In rare cases, lidocaine could potentially cause hypersensitivity reactions, confusion, or induce a transient alteration in heart rhythm.

Dual Energy X-ray Absorptiometry (DXA): You will be exposed to some radiation because DXA is an x-ray. The amount of radiation from the one DXA scan is equal to the amount of radiation in the natural environment if you were to walk around outside for 9 days.

ANTICIPATED BENEFITS RESULTING FROM STUDY PARTICIPATION

Taking part in this study may not personally help you, but your participation may lead to knowledge that will help others. Your participation may benefit science and humankind through the results of this study. It is possible that we may learn information that will help to improve prevention and/or therapy for diseases like obesity and obesity-associated complications, like insulin resistance and cardiovascular disease. The results may help patients in the future.

ALTERNATIVE PROCEDURES/OTHER TREATMENT AVAILABLE

You are not required to take part in this research study. This is not a treatment study. Your participation is entirely voluntary. You can refuse to participate now, or you can withdraw from this study at any time after giving your consent without affecting your healthcare/services or other rights. This will not interfere with your regular medical treatment if you are a patient.

The investigator(s) may stop your participation in this study without your consent for reasons such as: it will be in your best interest; you do not follow the study plan; or you experience a study-related illness or injury. You may be withdrawn from the study if laboratory tests suggest that it is not safe for you to continue.

GENETIC RESEARCH

Samples and information about you may be shared with others to use for research; however, we will not release your name. Because certain genetic information may be unique to an individual, it is possible that your genetic information could link research information to you.

It is possible that a commercial product, test or findings will be developed as part of this research. These may have value and may be developed and owned by the study staff, and/or others. If this happens, there are no plans to provide money to you.

What we learn about you from this sample will not be put in your health record. Your test results will not be shared with you or your doctor. No one else (like a relative, boss, or insurance company) will be given your test results. Health insurance companies and group health plans may not request your genetic information that comes from this research.

A new federal law, the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information obtained from this research.
- Health insurance companies and group health plans may not use your genetic information obtained from this research when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information obtained from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.
- All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

RESEARCH RESULTS

In the event new information becomes available that may affect the risks and/or benefits associated with this study or your willingness to participate in it, you and your physician will be notified so you can make a decision whether or not to continue your participation in this study.

Your study records and data will be stored in a secure database. The database will reside in a password protected secure website supported by the TVHS VA. Information in the database will only be available to study personnel. Your biological samples will be stored with a study ID label in a locked freezer. This label will not include any identifying information. Only key study staff will have access to your identifying information. All key study personnel involved in the design or conduct of this study will receive the required education on the protection of human participants.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent.

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

DISPOSITION OF RESEARCH DATA AND/OR SPECIMENS

This research study is anticipated to last 5 years. This study involves access of PHI data/limited data set for research as listed: Name, SSN for screening candidates (necessary for reimbursement), date(s) of lab tests and x-rays, and phone number for follow-up phone calls.

The research data will be stored in a RedCap database which is a password protected, secure web-based application maintained by the TVHS VA and retained in your research record in accordance with Veterans Health Administration (VHA) and Federal Records Control Schedule policies after the study is completed. Research data will be used/shared outside TVHS at the PI's office at Vanderbilt University Medical Center.

- Sensitive Research data (hard-copy data such as signed consent form, case reports forms):
  - PI's work space in VA TVHS
  - PI's office at VUMC
  - Research coordinators' office at VUMC
- Electronic sensitive research data
  - PI's folder on VA TVHS Server
  - PI's folder on VUMC Server
- The code linking your name with your ID number will be stored electronically on the VA's secure computer network.

- Data collected (per the HIPAA Authorization page 1) will be stored in the REDCap database on the TVHS computer server. A copy of this data collected will also be stored on the PI's TVHS Research Folder.

The research specimens will be stored at Dr. Bachmann's freezer in TVHS in Nashville. Specimens may also be stored in the Cardiovascular Core Lab at Vanderbilt University Medical Center before they are processed. Research samples will be retained indefinitely for future use, as applicable to this protocol, and may also be used in future research.

We may look at information collected in your medical record prior to the study and continue to view information in your records collected after the completion of the study. This is so we may view your medical chart before and after you complete the study.

Your samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, TVHS, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Should you qualify for future studies, we ask that you give us permission to contact you to discuss your interest and eligibility.

☐ Yes, I give my permission to be contacted in the future regarding other research projects I may qualify for.

☐ No, I do not give my permission to be contacted in the future regarding other research projects I may qualify for.

ADDITIONAL STUDY OPTION:

You may choose to opt into another study in which an additional 10ml of blood will be drawn at each of your two study visits. The blood will be used to study BNP levels using a different technique than is used in the main study.

☐ Yes, I wish to participate in the additional study and have an additional 10 ml of blood drawn at each study visit.

☐ No, I do not wish to participate in the additional study and have an additional 10 ml of blood drawn at each study visit.

CONTACT INFORMATION

If you have questions about this study, wish to express concerns or complaints about the research, or to report a research-related injury, you can contact:

- Study Coordinator: Grace Henderson (615) 936-5356
- Clinical Trials Manager: Cassandra Reynolds (615) 875-9854
- Principal Investigator (PI), Dr. Katherine Bachmann: (615) 875-9520

For 24-hour availability: (615)-835-8267, the automated voice will prompt you to enter your phone number in order for Dr. Bachmann to return your call. Once you have entered your phone number, please hang up.

If you have general questions about giving consent or your rights as a participant in this study or wish to discuss problems or concerns, offer input, or you want to make sure this is a valid VA study, or request information you can call the VA Tennessee Valley Healthcare System (VATVHS) Institutional Review Board Office at (615) 873-6076 or the Research and Development Service Office at (615) 873-6940.You may also contact the VATVHS Patient Advocate at 1-800-228-4973, extension 67225 or 1-800-876-7093 extension 22560, or (615) 873-7225 to discuss problems or concerns and ask questions not related to the consent process, offer input, or request information.

CONFIDENTIALITY AND PRIVACY

Your rights of privacy will be maintained in the following manner. Your medical records will be maintained according to this medical center's requirements and the Privacy Act of 1974. All information obtained about you during the research study will be kept as confidential as legally possible and will be accessible only to the investigators and members of the research team, the sponsor (when applicable), and any appropriate government agency. Research records, like any other hospital records, may be inspected by federal regulatory authorities, including the VA Office of Research Oversight, the VA TVHS Research Compliance Officer, the Food and Drug Administration (FDA), state regulatory authorities, and legally authorized parties.

Your permission to allow access to your medical information and a description of your rights under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) is addressed in a separate HIPAA Authorization document. By signing the separate HIPAA Authorization

form you agree to allow access, use and disclosure of your personal health information as described in the HIPAA Authorization form. By signing the consent form, you are voluntarily choosing to participate in the study as described below in this consent form.

STATEMENT & SIGNATURE OF PERSON AGREEING TO PARTICIPATE IN THIS RESEARCH STUDY:

Signatures. I agree to participate in this research project as described in this consent form. I will be given a signed copy of this consent form for my records. I have read or have had this consent form read to me.

- This study has been explained to me and all of my questions have been answered by the person obtaining consent. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. If I have questions later, I understand I can contact the researcher or a member of the research team.
- If I do not take part in this study, my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.
- I have been told my rights as a research subject, and I voluntarily consent to participate in this study. I have been told what the study is about and how and why it is being done. All my questions have been answered.
- I will receive a copy of this consent form and a copy will be forwarded to the VA Tennessee Valley Healthcare System Research Compliance Office.

SIGNATURES: (Note: ALL signatures and dates of signature below *are required* for legally effective research consent and HIPAA authorization.)

_____
Study Participant's SSN – ***full SSN required***

_____	_____	_____
Study Participant Name (Print)	Study Participant Signature	Date
_____	_____	_____
Name of person (Print) obtaining authorization and consent	Signature of person obtaining authorization and consent	Date