CONSENT FORM

Title of Research: The Diurnal Rhythm in Natriuretic Peptide Levels and Relationship with Nocturnal Blood Pressure

UAB IRBProtocol #: **IRB-300002114**

PrincipalInvestigator: Pankaj Arora, M.D.

Sponsor: UAB Division of Cardiology

GeneralInformation	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to understand how heart rhythms, hormonal levels, and blood pressure vary in obese and lean individuals. .
Duration & Visits	You will visit UAB three times, for a total of 27 hours.
Overview of Procedures	First, you will come for a 2-hour screening visit to perform blood tests and procedures. If you are eligible and enroll in the study, you will have a second, 1-hour visit in which you pick up meals and 24-hour blood pressure monitor. Third, you will participate in a 24-hour inpatient visit for observation. You will wear the 24-hour blood pressure monitor from 7 am to 7 am (24-hour) at home, followed by 24-hour in hospital stay at UAB.
Risks	The most likely risks and discomforts include the possibility of pain or bruising from the blood draw, loss of confidentiality, improperly prepared food, eating less than normal food amount, wearing 24-hour blood pressure device, fasting, and withdrawal symptoms for caffeine, alcohol and/or nicotine.
Benefits	You will not benefit from taking part in this study, but the results of this research study may help our scientific understanding.
Alternatives	The alternative is to not participate in this study.

Purpose of the Research

We are asking you to take part in a research study.

We are asking you to join this study because you are a healthy male between the ages of 18-50 who

has no history of heart disease, high blood pressure or diabetes or taking any medications for any of these conditions. The purpose of this study is to understand the diurnal rhythm (i.e., 24-hour) in natriuretic peptide (NP) levels (a hormone released from the heart) and its relationship with blood pressure in obese individuals [body mass index (BMI): 30 to 45 kg/m^2] as compared to lean individuals (BMI: 18 to 25 kg/m^2).

Diurnal rhythm is defined as 24-hour fluctuations which are typically controlled by light and temperature. NPs are hormones produced by the heart. Research has suggested the presence of diurnal rhythm in circulating NP levels in young healthy individuals. However, the proof of diurnal rhythm in NP levels in obese individuals is not known. Furthermore, obese individuals have relatively lower NP levels as compared to lean individuals. Differential diurnal rhythm of NP system between obese and lean individuals may be a reason of differential pattern of blood pressure in the obese and lean individuals.

We expect to enroll 40 lean and 40 obese individuals of both sex as matched group for this study at University of Alabama at Birmingham.

Study Participation and Explanation of Procedures

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

This study will take place at the UAB Clinical Research Unit (CRU), located on 15th floor in Jefferson tower building (625 19th Street S.) and an inpatient facility, located on the 8th floor of the Medical Education Building (1813 6th Ave S). After the end of 3rd visit, your participation in the study will be over.

Study Visit #1 (Screening Visit):
You will be asked to come to the CRU for the screening visit. It will take about 2 hours. During this visit, we will get your consent and perform the following tests and procedures to see if you are able to take part in the main study:

- Take your blood pressure three times. If your blood pressure is more than 140/90 mm Hg, you will not be able to continue in the study.
- Complete a questionnaire about personal information, past medical history, medications, family medical history, and sleep habits.
- Measure your height and weight.
- Draw about 25ml or 5 teaspoons of blood. We will do these tests on your blood: natriuretic peptide levels, a chemistry panel (electrolytes, kidney function and glucose), complete blood count, and a liver function panel.
- Schedule you to meet with a study nutritionist who will ask you about your dietary choices and practices.
- Give you a food log to take home and write down what you eat and drink for the next few days.

The study doctor will review the results of these blood tests and tell you if you can be in the study or not. If you cannot join the study, the study doctor will tell you the reason as well. We will suggest

follow-up with your primary care physician if there is any medical reason or abnormal blood test. If you can join the study and decide to continue in the study, we will ask for your convenient date and time, and schedule you for visits #2 and #3. Female subject will be asked to schedule their food pick and in-patient visit in their follicular phase of menstrual cycle (between 5th to 12th day of menstrual cycle).

If you can join for the study and decide to continue, we will ask you to eat a eucaloric diet for 5 days prior to the main study visit (i.e., 24-hour inpatient visit). The term eucaloric diet means the diet which has similar value in terms of calorie (a unit that measure energy from food). The diet will include of 3 meals a day (breakfast, lunch and dinner) and snacks and will be given to you by the UAB CRU. You will consume 2000 kilocalorie worth of meals during each day. While you are on this diet, we will ask you not to eat anything except water that is not given to you by the UAB CRU. We will give the meals to you at no cost. These meals will have all the nutrients required for a healthy diet.

Eligibility

Once eligibility is determined after review of the screening labs by the study investigators, you will be informed about eligibility by phone. If you are found eligible, you will be invited back for the 2nd (food, 24-hour blood pressure monitor and urine jar pick up) and 3rd/24-hour inpatient visit. You will be asked for your preferred dates for the 2nd and 3rd study visits. You will be instructed that 3rd visit date should be five days after the2nd visit.

Study Visit #2

You will be asked to pick up your meals, 24-hour blood pressure monitor, and 24-hour urine jar on scheduled date between 8 am to 4 pm from the CRU. It will last about 60 minutes. The instruction on how to wear, measure 24-hour blood pressure monitor and collect 24-hour urine will be provided by the study coordinator. You will be asked to wear 24-hour blood pressure device on last day of your diet (5th day) and collect 24-hour urine.

We will also ask you not to drink alcohol and caffeine-containing beverages (such as coffee, tea, soft drinks, or energy drinks). We will also ask you not to take part in heavy exercise.

Study Visit #3/24-hour inpatientvisit

Five days after 2nd visit, you will come for the 3rd visit. You will be asked to come to the CRU at 7 to 8 AM with overnight fasting. The study nurse or coordinator will take you to the in-patient facility located on the 8th floor of the Medical Education Building for 24-hour stay. We will ask you not to eat after midnight on the night prior to the visit. You may drink water and take your medications as you normally do.

When you arrive at the CRU, we will:

- Take your blood pressure.
- We will place an IV in one of your arms. This IV will be used to draw blood samples for the study. We will draw a blood sample to test for natriuretic peptide levels, other biomarkers, insulin, and glucose.

- After 1st blood draw, you will then proceed to your inpatient room where breakfast will be served.
- After this, we will observe you for 24 hours. You will have repeat blood draws obtained 5 times during day-time (8 am to 8 pm) and every 2 hours during night-time (10 pm to 6 am).
- As the hormone that we are studying can be affected by the sodium intake, you will be allowed to drink only distilled water that is provided by the study nurse during this visit.
- You will be provided distilled water to drink and 5 eucaloric meals without sugar and low-fat content following each of the first 5 blood draws.
- You will be asked to collect your urine in two different collectors; one in day-time and second in night-time.
- You will be asked to wear 24-hour blood pressure device during your inpatient stay.
- You will be discharged to home following the final blood draw.

Your de-identified private information and de-identified bio-specimens (private information and bio-specimens with all identifiers removed) may be used for future research studies without additional informed consent.

The results (including individual research results) generated during this study will not be returned toyou.

Risks and Discomforts

Risks of Blood Draw
You may have a small amount of bleeding or a bruise may develop when the IV line is put in place. Sometimes, a person feels faint or lightheaded when his/her blood is drawn. Rarely an infection can develop; it can be treated. Risk is lowered by keeping skilled person for blood draw.

Potentialbreachofconfidentiality
There is a slight risk that your private health information may be seen by others. But, safety measures will be taken to reduce such a problem.

Riskin food preparation
There is a small risk that food may not be prepared right. People who consume food that is not prepared right may experience nausea, vomiting, or diarrhea. However, the CRU metabolic kitchen follows correct policies and procedures to ensure food safety.

Risk and discomforts of eating less than normal food amount
There is a small risk that food quantity may be not sufficient to your daily need. People who consume less amount of food than they usually eat, may feel hungry.

Risk and discomforts of wearing 24-hour blood pressure device
You will be wearing a small device with regular blood pressure cuff for 24-hour at home prior to the last visit. There is a small risk that you may feel uneasiness while machine measure your blood pressure during day time. There is also a small risk that you may feel discomfort during sleep while

machine measure your blood pressure. There is also a possibility that you may feel sleepy on next day.

Risks of Fasting
For the study, you will be asked to fast (no food to eat) for approximately 8 hours-Overnight. Fasting may cause hypovolemia (a decreased volume of circulating blood in the body) and can make you dizzy, faint, or irritable.

Risks of caffeine, alcohol and/or nicotine withdrawal

1. Caffeine withdrawal: There is a small risk that people who take caffeine regularly, may show withdrawal symptoms like headache, fatigue or drowsiness, depressed mood or irritability, difficulty concentrating, and flulike symptoms such as nausea or muscle pain.
2. Alcohol withdrawal: There is a small risk of alcohol withdrawal in people who take alcohol regularly. They may show mild symptoms such as sleep disturbances and anxiety to severe and life-threatening symptoms such as delirium, hallucinations, and autonomic instability.
3. Nicotine withdrawal: There is a small risk of nicotine withdrawal in people who smoke or chew tobacco. They may show intense cravings for nicotine, tingling in the hands and feet, sweating, nausea and intestinal cramping, headaches, coughing, sore throat, insomnia, difficulty concentrating.

Benefits

You will not benefit from taking part in this study. The results of this research study may help our understanding of diurnal rhythm of NP levels in obese individuals and how it relates to the blood pressure.

Alternatives

Your alternative is to not participate in this research study.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

Information obtained about you for this study will be kept confidential to the extent allowed by law. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, Department of Medicine, Division of Cardiology and the Office for Human Research Protections (OHRP). The information from the research may be published for scientific purposes; however, your identity will not be given out.

What protected health information may be used?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Your consent form will not be placed in your medical record at UAB Health System or Children's of Alabama. However, if you are receiving care or have received care within the UAB health system (outpatient or inpatient), results of research tests or procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing medical record.

If you have never received care within this health system (outpatient or inpatient), a medical record will be created for you to maintain results of research tests or procedures.

Results of research tests or procedures may be placed in your medical record. All information within your medical record can be viewed by individuals authorized to access the record.

A description of this clinical trial will be available on https://clinicaltrials.gov/ct2/show/NCT03834168?term=diurnal+rhythm&cond=natriuretic+peptide&rank=1 , 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.

Who may use and give out information about you?
Information about your health may be used by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?
All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research at UAB.

Information about you and your health which might identify you may be given to:
- the Office for Human Research Protections (OHRP)
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to research staff, nurses and physician to carry out the research study.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally 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 that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

Whatif I decide not to give permission to use and giveout my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution.

You may be removed from the study without your consent if the sponsor ends the study, if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study.

Payment for Participation in Research

You will be paid $25 for screening visit, $10 for 2nd visit, $65 for 24-hour ambulatory blood pressure, and $200 for 3rd visit in about 4 weeks after study visit. Ask the study staff about the method of payment that will be used for this study (e.g., check, direct deposit).

Paymentfor Research-Related Injuries

UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

Significant New Findings

You will be told by your doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional Research

Please note: This section of the consent form is about optional research that is being done with people who are taking part in this study. You may take part in this optional research if you want to. You can still be a part of this study even if you say no to take part in any of the optional research.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

In addition, we would like your permission to contact you about being in future research projects related cardiovascular and metabolic diseases. Based upon result of this visit and test results, we may contact you by phone or in writing about future studies.

You can say no to participate in these studies.

Do you agree to let us contact you in the future about participating in other studies related to cardiovascula

_____I agree to allow you to contact me about other studies. (Check and initial)

_____I DO NOT agree to allow you to contact me about other studies. (Check and initial)

Genetic Testing

We would like to request your permission to collect ½ tablespoon of whole blood to extract DNA and store that for future studies. We are not going analyze your DNA study information for this protocol. The DNA that composes of your genes will be analyzed and that data, which is referred to your genotype or complete genetic makeup, compared to your phenotype, which consists of your observable traits, characteristics, and diseases in the future.

There are multiple genes involved in the regulation of human blood pressure. Until recently, no common genetic variants had been found which were related to human blood pressure. A genetic variant is a change in a particular gene that may affect the health of the person who has it. Recently, researchers have discovered a genetic variant which is present in about 1 out of 10 people and is related to blood pressure and to levels of natriuretic peptides.

We may pursue to study these genetic variates in the future. The future research related to these genetic variates may be conducted by Dr. Pankaj Arora or other researchers after the IRB's approval for their research. However, your identity relates to these specimen will be coded and only Dr. Pankaj Arora will have access to it.

The results related to these future studies will not be disclosed to you or your doctor. Initial your choice below:

_____I agree to allow you to store DNA to test for genetic variants.

_____I DO NOT agree to allow you to store DNA you to test for genetic variants

Gene Expression

We would like to request your permission to collect ½ teaspoon of whole blood in special tubes called PAXgene tube to extract RNA and store that for the current study during 24-hour inpatient visit for each time-point. Through RNA extraction, we are going to see gene expression of certain natriuretic peptide family of genes in whole blood. The principal role of RNA is to act as a messenger carrying instructions from DNA for controlling the synthesis of proteins.

Do you agree to let us store RNA from your blood and contact you for the future studies related to genetic variants?

Initial your choice below:

_____I agree to allow you to store RNA to test for its expression in the current study.

_____I DO NOT agree to allow you to store RNA to test for its expression in the current study.

Future Research Use of Private Information and/or Biospecimens

We would like your permission to keep your private information (data containing personal information) and blood samples collected in this study for future research. The future research may be similar to this study or may be completely different. Your private information and blood sample will be stored indefinitely or until used.Your private information and blood samples will be labeled with a code that only the Dr. Pankaj Arora can link back to you. Results of any future research will not be given to you or your doctor. You can take part in this study even if you decide not to let us keep your private information and blood samples for future research.

If you give us permission now to keep your private information and blood samples, you can change your mind later and ask us to destroy it. However, once we have analyzed your private information and blood samples, we may not be able to take it out of our future research.

Future research use of your private information and blood samples will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your private information and blood samples. Allowing us to do future research on your private information and blood samples will not benefit you directly.

Initial your choice below:

_____I agree to allow my samples to be kept and used for future research on heart. (Check and initial)

_____I do not agree to allow my samples to be kept and used for future research. (Check and initial)

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, you may contact Dr. Nirav Patel and Dr. Pankaj Arora. They will be glad to answer any question. Dr. Patel's number is 205-934-6058 and Dr. Arora's number is 205-936- 6630. Dr. Patel may also be paged after hours at 205-435-5866.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855- 860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

Legal Rights

You are not waiving any of your legal rights by signing this informed consent document.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

Signature of Participant Date

Signature of Person Obtaining Informed Consent Date