The University of Texas Southwestern Medical Center at Dallas
Parkland Health & Hospital System
Children's Medical Center
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital of Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	The Role of Aldosterone on Exercise Pressor Reflex in Hypertension Experiment E: Effects of MR antagonists on EPR in EH and PA.
Funding Agency/Sponsor:	National Institute of Health
Study Doctors:	Wanpen Vongpatanasin, MD, Jarett Barry, MD; Hamza Lodhi, MD; Mu Huang, PhD.
Research Personnel:	Martha Cruz, Ursa Bezan Petric.

You may call these study doctors or research personnel during regular office hours at 214-648-3188. At other times, you may call them at 214-645-8424.

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

Why is this study being done?
The study is being done to find out if signals from the muscles cause the nerve activity and blood pressure to increase too much during exercise in patients with high blood pressure and high aldosterone hormone (a hormone release from adrenal gland above your kidneys that can increase blood pressure).

Why is this considered research?
This is a research study because we want to find out if signals from the muscle cause nerve activity and blood pressure to increase too much during exercise in patients with high blood pressure and high levels of a hormone aldosterone.

The following definitions may help you understand this study:

- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you have high blood pressure from high aldosterone hormone or have high blood pressure with normal aldosterone hormone.

Do I have to take part in this research study?"
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
About 30 people (15 with high blood pressure and normal aldosterone level, 15 with high blood pressure and high aldosterone level) will take part in this study at UT Southwestern or Parkland Health & Health System.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

Screening Procedures
To help decide if you qualify to be in this study, you will have the following tests and/or evaluations.

- Physical exam, medical and surgical history, history of mental illness, and substance abuse;
- Vital signs;
- Blood tests;
- Demographic information (age, sex, ethnic origin)
- Pregnancy testing (urine test for female only)
- Research Personnel will provide diet containing approximately 2 grams of sodium per day for 7 days.
- If you are taking medications for high blood pressure, you will be asked to

stop your medications for 1 week.
- One week after you stop your medications and take 2-gram sodium diet we have provided, you will be asked to come our laboratory.

Group Assignment

If the researchers believe you can take part in this study, you will be asked to take Amlodipine or Eplerenone. You may receive Amlodipine or Eplerenone first. Then, taking study drugs for 8 weeks you will be asked to stop the first drug and start the second drug for 8 weeks. The order of the treatment is in random order. The study assignment is made in advance by a process similar to flipping a coin. You have a 1 in 2 chance of receiving Amlodipine or Eplerenone first.

The group you will be in is decided by Investigation drug service at the University of Texas Southwestern Medical Center. Neither you nor the researchers will be allowed to choose which group you are assigned to.

Neither you nor the researchers will know which group you are in. However, the sponsor will release the information about your assignment to the researchers if it is needed for your safety.

Study Medication/Intervention

If you decide to participate in this study you will be asked to either:

- Take Amlodipine 1 tablet once a day for 8 weeks first, then stop Eplerenone 1 tablet once a day for 8 weeks.

OR

- Take Eplerenone 1 tablet once a day for 8 weeks first, then take Amlodipine 1 tablet once a day for 8 weeks.

Procedures and Evaluations during the Research

Visit 1 (At 0 week; 4 hours),

- You will be asked to collect urine for 24 hours to check sodium in urine the day before the first visit while you consume 2-gram sodium diet.
- You will be asked to do a questionnaire to assess your dietary intake.

- When you return urine samples, research personnel will place a thin plastic tube in a vein in your arm.
- Research personnel will collect four tablespoons of blood from the tube in your arm for the research purpose.
- You will have an electrocardiogram (ECG) to measure electrical activity in the

heart.

- An arm cuff will be placed on the upper arm to measure your blood pressure.
- A tiny needle will be placed in a nerve in your right leg to measure nerve signals.
- You will have a sonogram on your arm to measure blood flow in your arm
- You will have 2 sticky patches placed on the same arm to measure muscle activity or electromyogram (EMG) during arm exercise.
- Research personnel will strap one of your hands to a bicycle pedal and move the other arm pedal to move your arm in circle while you keep your arm muscle completely relaxed for 5 minutes.
- Then, you will be asked to move your hand on the pedal in circle without assistance from research personnel for 5 minutes.
- After waiting for your nerve activity and blood pressure to return to normal for 30 minutes, you will be asked to do handgrip exercise intermittently at the rate of 20 times per minute at 30 % and 45% of your maximal strength each for 3 minutes while we monitor your blood pressure, your nerve activity, muscle activity, and blood flow in your arm.
- After waiting for your nerve activity and blood pressure to return to normal for 30 minutes, you will be asked to use your hand to hold a handgrip bar constantly without relaxing your hand at 30 % of your maximal strength for 2 minutes.
- Five seconds before you stop exercising, a cuff around your upper arm will be inflated to stop blood flow to your arm for 2 minutes.
- After the cuff is released, we will continue to monitor your nerve activity, and blood flow in your arm for 5 minutes.
- After waiting for your nerve activity and blood pressure to return to normal for 30 minutes, you will be asked to put your hand in iced water for 2 minutes, while we monitor your blood pressure, your nerve activity, and blood flow in your arm.
- You will then be started on the first study drug (Amlodipine or Eplerenone)

Visit 2: (2 weeks later:30 minutes)

- Two weeks after you start the first study drug, research personnel will check your blood pressure and adjust your medications according to your blood pressure.

Visit 3: (2 weeks later:30 minutes)

- Four weeks after you start the first study drug, research personnel will check your blood pressure and adjust your medications according to your blood pressure.

Visit 4: (2 weeks later:30 minutes)

- Six weeks after you start the first study drug, research personnel will check

your blood pressure and adjust your medications according to your blood pressure.

Visit 5: (2 weeks later:30 minutes)

- You will be asked to stop your BP medications and take diet containing approximately 2 grams of sodium per day for 7 days before the study
- You will be asked to collect urine for 24 hours to check sodium in urine the day before the second study while you consume 2-gram sodium diet.
- When you return urine samples, research personnel will collect four tablespoons of blood from the tube in your arm for the research purpose.
- The same procedure in visit 1, will be repeated.
- You will then be started on the second study drug (Eplerenone or Amlodipine).

Visit 6: (2 weeks later:30 minutes)

- Two weeks after you start the second study drug, research personnel will check your blood pressure and adjust your medications according to your blood pressure.

Visit 7: (2 weeks later:30 minutes)

- Four weeks after you start the second study drug, research personnel will check your blood pressure and adjust your medications according to your blood pressure.

Visit 8: (2 weeks later:30 minutes)

- Six weeks after you start the second study drug, research personnel will check your blood pressure and adjust your medications according to your blood pressure.

Visit 9: (2 weeks later:4 hours)

- You will be asked to stop your BP medications and take diet containing approximately 2 grams of sodium per day for 7 days before the study
- You will be asked to collect urine for 24 hours to check sodium in urine the day before the second study while you consume 2-gram sodium diet.
- When you return urine samples, research personnel will collect four tablespoons of blood from the tube in your arm for the research purpose.
- The same procedure in visit 1, will be repeated.
- End of study.

- In a separate optional visit, you will be asked to pedal on a stationary bicycle. It will become harder to pedal the longer you exercise. You will breath into a mouthpiece (like a snorkel) or a facemask so we can measure the air you

breathe. You will be connected to an EKG and blood pressure monitor and will be monitored during the test. This will help us ensure you are safe and study how the heart responds to exercise and determine your exercise capacity. During the second half of the test, an echocardiogram will be performed while you are pedaling on a reclining bike.

The blood tests and blood flow tests done in this study are designed for research, not for medical purposes. They are not useful for finding problems or diseases. Even though the researchers are not looking at your blood tests and blood flow tests to find or treat a medical problem, you will be told if they notice something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the blood tests and blood flow tests done in this study are not for medical purposes, the research results will not be sent to you or to your regular doctor.

How long can I expect to be in this study?
The study will last for approximately 16 weeks. Visits 1 and 9 will require 4 hours of your time and visits 2 to 8 will requires 30 minutes of your time at each visit. There will be no follow-up visit after the end of study.

You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?

Study Procedure/Intervention
Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.
-Eplerenone may cause some, all or none of the side-effects listed below.

	Frequent 30% of subjects	Occasional Less than 5% of subjects	Rare Less than 1% of subjects
Serious		High potassium	Allergic reaction
Less Serious		Dizziness, fatigue	Low blood pressure,
Minor			

- Amlodipine may cause some, all or none of the side-effects listed below.

	Frequent 30% of subjects	Occasional Less than15% of subjects	Rare Less than 1% of subjects
Serious			Allergic reaction
Less Serious		Swelling of the feet, constipation,	Low blood pressure, dizziness

		headache, elevated heart rate, heart pounding	
Minor			Increase in size of the gums

-Placement of a needle in a nerve: One out of ten may have muscles soreness, pins-and-needles feeling , increased sensitivity to touch, leg or arm numbness or weakness one or two days after the experiment. However, these symptoms usually resolve within 2-3 weeks after the procedure. We will ask you not to exercise your arm or leg within 24 hours after procedure. Permanent damage to the nerve has not been reported to occur from this procedure.

-Blood pressure cuff inflation: The blood pressure cuff will squeeze your arm tightly. However, any discomfort will stop as soon as the pressure in the cuff is released.

-Placement of a thin tube in a vein: You may experience discomfort, bleeding, and/or bruising. You may feel dizzy or faint. On a rare occasion, an infection may develop at the site where the tube was placed. There is a small risk that a blood clot will form or the thin plastic tube (catheter) will break.

-Blood samples: You may experience discomfort, bleeding, and/or bruising. You may feel dizzy or faint. On a rare occasion, an infection may develop at the site where the blood was collected.

-Handgrip exercise: You may experience discomfort or aching in your arm but the sensation should stop quickly after you stop exercise.

-Cardiopulmonary testing*:* With any type of exercise testing, there exists the possibility of injury or discomfort. Hard exercise may cause strain or injury to the muscles, bones and joints. During testing, the risk of having a heart attack or even dying goes up slightly, however the risk during any given session in an apparently healthy person is less than 1/100,000 tests. Exercise tests may also occasionally be accompanied by abnormal blood pressure, nausea, fainting, muscle soreness, joint and bone injury, and in rare instances, heart attack, stroke, or death. Every precaution will be taken to minimize these risks by evaluating your health and fitness status throughout the study. A licensed physician will be immediately available.

Yes, I agree to have the optional cardiopulmonary testing during this study.

Initials Date

Patient

No, I do not agree to have the optional cardiopulmonary testing during this study.

Initials Date

Patient

Loss of Confidentiality

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

Risks of Blood Drawing

Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely.

You will have 14 tablespoons of blood collected because you are in this research study.

Other Risks

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

How will risks be minimized or prevented?

The research laboratory is fully equipped to handle any bad side effects. Dr. Vongpatanasin is a high blood pressure specialist and cardiologist with extensive experiences in performing the research procedures in this study. Your heart rate, electrocardiogram, and blood pressure will be monitored constantly during the study. Emergency equipment, in the event of that your heart stops or you stop breathing, is immediately available with highly trained staff.

What will my responsibilities be during the study?

While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.

- Report to the researchers any injury or illnesses while you are on study even if you do not think it is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?

If you agree to take part in this study, there will not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research.

We hope the information learned from this study will benefit others with high blood pressure in the future. Information gained from this research could lead to better treatment of high blood pressure during exercise.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for high blood pressure. Instead of being in this study, you can receive high blood pressure treatment from your regular doctor.

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

You will be paid $ 1,000 for participation in completing the entire study. However, if you stop taking part in this study or are withdrawn by the research team, you will paid according to number of weeks participated the study of $ 60 per week. Your Social Security Number (SSN) will be given to The University of Texas Southwestern Medical Center in order to process your payment as required by law. This information will remain confidential unless you give your permission to share it with others, or if we are required by law to release it.

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

If you are an employee of UT Southwestern, your payment will be added to your regular paycheck and income tax will be deducted.

UT Southwestern, as a State agency, will not be able to make any payments to you for your participation in this research if the State Comptroller has issued a "hold" on all State payments to you. Such a "hold" could result from your failure to make child support payments or pay student loans, etc. If this happens, UT Southwestern will be able to pay you for your taking part in this research 1) after you have made the outstanding payments and 2) the State Comptroller has issued a release of the "hold."

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

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

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

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

You retain your legal rights during your participation in this research

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

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

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

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

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

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

- Your medical problem becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?

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

- National Institute of Health
- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board.
- Quest Diagnostic Laboratory

A description of this clinical trial will be available on http://www.trials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search the Web site at any time. In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Whom do I call if I have questions or problems?

For questions about the study, contact Dr. Vongpatanasin at 214-648-2103 during

regular business hours and at 214-645-8424 after hours and on weekends and holidays.

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

SIGNATURES:

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

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.

- You have freely decided to participate in this research.
  You understand that a copy of this signed consent document, information about this study and the results of any test or procedure done may be included in your medical record and this information may be available to health care providers, and authorized persons including your insurance company.
- You understand that you are not giving up any of your legal rights.

_____

Participant's Name (printed)

_____ _____AM/PM

Participant's Signature Date Time

_____

Name of person obtaining consent (printed)

_____ _____AM/PM

Signature of person obtaining consent Date Time

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

_____	_____	_____	_____	_____
Signature of Interpreter	Printed Name of Interpreter	Date	Time	AM/PM