Neuropeptides in Human Reproduction

NCT04975334

July 29, 2025

Mass General Brigham

Research Consent Form
Certificate of Confidentiality Template
Version Date: November 2022

Subject Name:

MRN or DOB:

Subject Identification

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Protocol Title: Neuropeptides in Human Reproduction

Principal Investigator: Stephanie Seminara, MD

Site Principal Investigator:

Description of Subject Population: Men and women with hypogonadotropic hypogonadism (18-75 years), Healthy and variant-carrying men (18-60 years), Healthy and variant-carrying women (18-40 years)

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

We are asking you to be in a research study. This form will tell you what you should expect if you agree to be in the study. You will find more information about each of the following points later in this form.

It is your decision whether or not to join the study. We are asking you to be in this study either because you are a healthy volunteer, because you have been diagnosed with a form of hypogonadotropic hypogonadism (such as low testosterone), or because you are enrolled in the Mass General Brigham Biobank Study. We are doing the research to learn more about the relationship between reproduction and a hormone called dynorphin.

If you agree, you will come to MGH for one screening visit and one main study visit. During the study visit, you will have small amounts of blood drawn periodically for three hours, and you will

receive a medication called naloxone. The screening visit takes about one hour, and the study visit takes approximately 5 hours.

The main risks of being in the study are associated with the administration of naloxone and of frequent blood sampling.

You will be paid up to $540 by check for taking part in this research study. You will find more information about the payment amount for each visit and a plan if you do not complete all study visits later in this form.

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Stephanie Seminara, MD is the person in charge of this research study. You can call her at [redacted] (Monday through Friday from 9 a.m. to 5 p.m.). Dr. Seminara can be paged by calling [redacted] and entering pager #[redacted] She is available 24 hours a day, 7 days a week to answer questions about this research study.

You can also call Margaret Lippincott, MD at [redacted] (Monday through Friday from 9 a.m. to 5 p.m. with questions about this research study. Dr. Lippincott can be paged by calling [redacted] and entering pager [redacted]. She is available 24 hours a day, 7 days a week to answer questions about this research study.

If you have questions about the scheduling of appointments or study visits, call [redacted] or email the study coordinator at mghreproendoresearch@mgb.org.

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

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

Why is this research study being done?

We are doing this research study to learn more about the human reproductive system. We know that a specific part of the brain called the hypothalamus makes the hormone GnRH (short for "gonadotropin-releasing hormone"). A hormone is a chemical that the body makes naturally. Women need GnRH to make estrogen, to have normal menstrual cycles, and to become pregnant, and men need GnRH to make testosterone and to father a child.

The purpose of this study is to try to understand how a chemical called dynorphin (pronounced "dy-NOR-fin") controls the amount of GnRH that our body makes.
Dynorphin is a type of chemical called an opioid, which is naturally made in the body. Opioids are best known for decreasing pain, but they also affect the activity of the reproductive system. We want to know what happens to reproductive hormones if we stop dynorphin from working. As part of this study, you may receive a drug called naloxone that blocks the activity of dynorphin.

Naloxone
Naloxone is approved by the FDA to treat overdoses of opiates such as heroin, oxycodone, morphine, and opium. Naloxone is not approved by the FDA to study reproductive hormones; however, we are able to give naloxone to our participants off-label at the discretion of the study doctors or study nurses, meaning that our medical professionals use their clinical judgement to give naloxone safely outside of its typical use.

Who will take part in this research?

We are asking you to be in this study either because you are a healthy volunteer, because you have been diagnosed with a form of hypogonadotropic hypogonadism (such as low testosterone), or because you are enrolled in the Mass General Brigham (MGB) Biobank Study.

About 152 people will take part in this research study. About 48 people with hypogonadotropic hypogonadism, 40 individuals from the MGB Biobank, and 64 healthy volunteers will take part in this study, all at the Massachusetts General Hospital (MGH).

The National Institute of Child Health and Human Development (part of the National Institutes of Health) is paying for this research to be done.

What will happen in this research study?

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

Taking Part In Other Research Studies

You need to tell us if you have taken part in, or plan to take part in, any other research study while you are in this study. Also, please let us know about any medical activites, such as a new medicine or a trip to the doctor, during this study. This is for your safety.

VISIT 1: Screening Visit (about 1 hour)

During this visit, we will do some tests and procedures to see if you qualify to take part in this research study. A study doctor or study nurse will review the information collected during screening. If you don't qualify for this study, we will tell you why. The screening visit can take place either at MGH or remotely. Remote activities may be done over the phone and/or at a blood drawing laboratory that is near you.

If you are a male, we will ask you to fast (no food or drink, other than water) for at least 8 hours before your screening visit (overnight). This is important to make sure that we accurately measure your testosterone level.

At this Screening visit, we will:

- Ask you about your medical history.
- Conduct a physical exam and measure your height and weight. (If remote, this will be done at your first in person visit.)
- Draw a blood sample (about 1 tablespoon) to measure hormone levels and make sure you are healthy enough to participate in the study.
- Do a blood pregnancy test, if you are a woman who can become pregnant (if you have a uterus and at least one ovary). Pregnant women cannot take part in this research study.
- Do a urine drug test. During this study, we will test your urine for certain drugs, including illegal drugs (e.g., cocaine, heroin). If your urine shows you have taken any of these drugs, you can't be in this study. The results of the urine drug test will not become part of your medical record. These test results will, however, remain part of your study record.

Stopping Your Current Medications

If you are taking medications that affect the reproductive system, we might ask you to stop taking them during your participation in the study. For example, birth control pills (oral contraceptives) and certain pain medications can affect the reproductive hormones that we are measuring. The study team will ask about your current medications and let you know if washout from any of them is required for you to participate in the study. Stopping the medicine means not taking any tablets, patches, creams or using vaginal rings. This "washout period" allows these medications to leave your body before you begin Visit 2.

If this is applicable to you, you may decide whether you want to do the washout required to participate in this study. We suggest that you discuss the washout with your prescribing physician(s) before you stop taking your medication. The doctors for this study, in most circumstances, will not be part of your regular healthcare team. Therefore, one of the study doctors or a study nurse may speak with your prescribing physician(s) to determine if it is appropriate for you to stop taking any medication. Without your regular medications, certain medical conditions or symptoms controlled by your medication(s) may get worse. If this happens, please call one of the study doctors at the phone number provided in this consent form.

Additionally, regular users of marijuana will be asked to abstain from use for at least two weeks prior to Visit 2.

VISIT 2: MGH Study Visit (up to 5 hours)

If you qualify for the study, you will come to the hospital for Visit 2. Visit 2 will last up to 5 hours.

If you are male, we will ask you to fast overnight on the night before your study visit and until the end of your study visit. This means that you cannot eat any solid food and cannot drink anything apart from water once your fast begins. We will give you lunch as soon as your study visit is over. This fasting is important to ensure that we accurately measure your testosterone levels. We encourage you to be well hydrated for your visit. You may take your usual medications during this fasting period.

At Visit 2, we will:

- Do a urine pregnancy test, if you are a woman who can become pregnant.
- Place a thin, plastic tube called an intravenous line (IV) in your arm. The IV allows us to take many blood samples without having to use a needle each time. The IV will stay in your vein for the entire study visit.
- Frequently draw a small amount of blood for no more than 3 hours; the shortest time frame between blood draws is 10 minutes.

- During this visit we will draw around 65mL (a little more than a quarter of a cup) of blood.
- Give you naloxone through an IV.
- Use EMLA cream at any needle insertion site to ease discomfort during this visit.

After the last blood draw, we will remove the IV and you can go home.

If you stopped taking any medications for this study, you may restart the medications after the study visit. We suggest that you discuss restarting your medications with your prescribing physician(s).

Stopping the Study Early

You may decide to stop taking part in the study for any reason. Also, the study doctor may decide to stop your participation in the study, without your permission.
You might be asked to stop taking part because:

- The study doctor thinks it is best for you to stop taking the study drug.
- The study doctor thinks it is best for you to stop participating in the study.
- You can't make the required study visits.
- We stop doing the study for other reasons.

If this happens, the study doctor will explain why you need to stop taking part in the study.

Review of Medical Records

We might access your medical records while you are participating in this study. Any access would end within about 4 weeks of the last study activity you complete. Some reasons we would access your records are listed below.

Mass General Brigham has an electronic system that lets your study doctors know if you are admitted to a Mass General Brigham Hospital, or if you visit a Mass General Brigham Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study. So, we may review these records to determine if this event will affect your participation in the study.

We may also review your medical records to collect information about your health and if we need more information to assess whether you are eligible to participate and healthy enough to complete all study activities. We may ask you to provide medical records from outside hospitals or doctors.

We will ask you to sign a medical record release form to allow the outside hospital or doctor to send us records.

We may access your medical records to ensure that study-related charges are billed correctly.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. We will access your medical record to make and update this notation. Information from the research that relates to your general medical care may be included in the record (for example, list of allergies, results of standard blood tests done at the hospital labs).

Please ask a study doctor or study nurse if you have any questions about what information will be included in your electronic medical record.

Use of your Samples and Research Information

All of your samples will be stored in our research lab and labeled with a code that links the sample to you, but the samples will not be labeled with your name, date of birth, or any other identifiable information.

Your samples will be saved indefinitely. Research is an ongoing process and we will continue to use your samples and data in the future. We cannot give you an exact date when we will either destroy or stop using your samples and data.

If you want to withdraw your samples from further research, you should contact Dr. Seminara or the study staff in writing and your samples will be destroyed. We will retain all information we have already collected, and this information may continue to be used in our research.

If you participate in other research studies in the Reproductive Endocrine Unit (past or future), we may access information from that study to better understand data generated from this study.

How may we use and share your samples and health information for other research?

The samples and information we collect in this study may help advance other research on general health and disease. If you join this study, we may remove all information that identifies you (for example your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible for other researchers to link the information or

samples back to you. We will label all your study materials with a code instead of your name. They key to the code connects your name to your study information and samples. The study doctor will keep the key to the code here at Mass General Brigham and will not share it with our research collaborators. No one outside of Mass General Brigham will be able to link your identity to your study data or samples. Data and/or samples may be shared with investigators, at other academic institutions or non-profit institutions, or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

We may store and share your identifiable samples and study information with researchers at Mass General Brigham for other research related to general health and disease.

In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that analyze data and collect the results of research studies. We may send samples or information to these banks. These central banks will store your coded data and samples and may give them to other researchers to do more studies. We do not think that there will be further risks to your privacy and confidentiality by sharing your samples and data with these banks. However, we cannot predict how this information will be used in the future. The samples and data will be sent with only your code number attached. Your name or other directly identifiable information will not be given to central banks. There are many safeguards in place to protect your information and samples while they are stored in repositories and used for research.

Research using your samples is important for the study of virtually all diseases and conditions. Therefore, the sample/data banks will provide study data for researchers working on any disease.

Will you get the results of this research study?

No. The research study we are doing is only a next step in understanding reproductive disorders. Some of the tests in this study are run in clinical laboratories. Results of these tests may be placed in your medical record. Other tests in this study are run in research laboratories. These test results will not be placed in your medical record or returned to you or your medical doctor; they are not intended to influence your medical treatment.

If a study doctor or study nurse is concerned about any findings while you are participating in the study, we will alert you and recommend that you follow up with an appropriate clinical provider.

What are the risks and possible discomforts from being in this research study?

Risk of Allergic Reaction

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call a study doctor right away. If you are having trouble breathing, call 911 immediately.

Risks of Taking Naloxone

There are no known side effects of naloxone in healthy adults who are not taking opiate drugs.

In adults who take opiate drugs, the risks of naloxone can include (between 1 and 10 out of 100):

- Pain
- Sweating
- High blood pressure
- Irritability

In adults who are addicted to opiate drugs, naloxone can cause:

- Seizures
- Nausea
- Vomiting
- Diarrhea

Risks of EMLA Cream

EMLA is a numbing cream containing lidocaine and prilocaine. There is very little risk associated with using EMLA, but some mild, transient skin reactions have been reported.

Risks of Taking Naloxone to an Embryo, Fetus, or Breastfeeding Infant

The effect of naloxone on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Breastfeeding

- Trying to become pregnant

If you are a menopausal woman and have not had a period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus with or without the ovaries), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), or transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before receiving naloxone.

If you think you might be pregnant during the study, you must tell the study doctor immediately.

Risks of Intravenous (IV) Lines and Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples or where we put in an IV. There is a small risk of feeling fatigued, lightheadedness, fainting, or infection. The IV catheter may cause bleeding, bruising, irritation, swelling, clotting in the vein, leakage of medication or solution into the surrounding tissues, and possibly infection at the insertion site of the catheter. There is a slight chance that an IV line may stop working. If an IV line stops working, we will put in a new one. The place where the IV is put into your arm is often covered with an adhesive bandage or adhesive tape. You might have some temporary skin redness, irritation, or discomfort at the IV site, especially if you have sensitive skin.

Risks of Stopping Current Medications

If you are asked to stop taking your current medication, you might experience the return of some symptoms that are controlled or mitigated by these medications. However, we do not expect our participants to experience a prolonged recurrence of symptoms, and we expect any short-term symptoms to be rapidly reversible. If this happens, tell the study doctor or study nurse. If you stop taking oral contraceptives, or another form of birth control, the likelihood of becoming pregnant also increases, unless you are abstinent or use another highly effective form of contraception. All subjects who are able to become pregnant are advised to use an alternate form of birth control while on the study.

What are the possible benefits from being in this research study?

You will not benefit from taking part in this research study. However, people with reproductive disorders may benefit in the future from what we learn in this study.

Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

We will pay you up to $540 if you complete this study. This includes:

- Screening: $40
- MGH study visit: $500

Depending on the timing and length of your visits, we may give you meals during your study visits. We will give you a parking coupon to pay for your parking in the hospital garage during study visits. We may also pay or reimburse you for some of your travel expenses.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

The Reproductive Endocrine Unit is providing the study drug(s) at no cost to you. Study funds will pay for certain study-related items and services.

We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research

- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other researchers within or outside Mass General Brigham, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

_____
Print Name

_____ _____ _____
Subject Signature Date Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____
Print Name

_____ _____ _____
Signature of Study Doctor or Person Obtaining Consent Date Time (optional)

Permission for Future Contact

We may want to contact you about research in the future. Do you give permission for us to contact you about other research opportunities?

☐ YES, I give permission to be contacted about future research.

☐ NO, I do NOT wish to be contacted about future research.

_____

Print Name

_____ _____ _____

Subject Signature Date Time (optional)

Consent Form Version Date: 07/28/2025