**Principal Investigator:** **Alex Polotsky, MD**
**COMIRB No:** **15-0474**
**Version Date:** **06-Oct-2020**
**Study Title:** **Dysregulation of FSH in Obesity: Functional and Statistical Analysis**

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You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you do not understand before deciding whether or not to take part.

**Why is this study being done?**
This study plans to learn more about the relationship between fertility and obesity. You are being asked to be in this research study because you are a woman 21-39 years old with a body mass index (BMI) of either: between 18.5 and 24.9 or greater than 30.

**Other people in this study**
Up to 120 people from your area will participate in the study.

**What happens if I join this study?**
If you join the study, your research visit(s) will be completed at the Clinical Translational Research Center (CTRC) at the University of Colorado, Denver.

**Screening Visit:** This visit will take about 1 hour.

- You will have an examination of your skin, head, mouth, and neck as well as your heart and stomach. You will also have a pelvic exam: a visual and physical examination of your reproductive organs. This means that your doctor will wear lubricated gloves and insert two fingers into your vagina while using the other hand to feel your abdomen. This is to check for irregularities in your uterus or ovaries. *
- You will have someone listen to your heart and examine your legs for swelling, and check your vital signs (temperature, pulse, and blood pressure)*. They will also measure your hip and waist circumference.
- You will be asked about your menstrual status, medical history and your medication history.
- About 6 teaspoons of blood will be taken from a vein in your arm.
- We will calculate your BMI.
- You will be provided home ovulation test strips and instructions for use. These kits will help us better predict the timing of your period and will help us schedule your study visit. Use of these kits will involve dipping a test stick in urine each day for several days to see if it changes color. You will then notify the study coordinator once you see a positive result.
- You will be provided with an at home fecal collection kit to bring back at the study visit in the Inpatient CTRC. Please bring back the most recent fecal sample you can using the at home collection kit. Please follow the kit instructions.

*These procedures might occur at the study visit instead of the screening visit.

If your screening visit laboratory tests appear normal and the investigator determines you are eligible, you will be asked to come in for a 26-hour visit. This will be scheduled to correspond with days 3-6 of your menstrual cycle.

**Study Visit**

**Day 1:** The study will begin at 1:30pm in the In-Patient CTRC with the placement of an IV catheter, a pregnancy test and you will be provided with a regular patient room at University of Colorado Hospital. We will draw small volumes of blood (3-4mL) every 10 minutes for 10 hours through this IV. At approximately midnight, we will give you the study drug Cetrorelix (3 mg) subcutaneously, right under the skin usually in the stomach area. During this day we will also collect your urine four times throughout the day. Your meals will be provided by the hospital cafeteria during your entire stay in the CTRC.

**Day 2:** At 6am, we will start collecting small volumes of blood again for 10 hours. You will be given the study drug Cetrorelix (.25 mg) subcutaneously. You will also be given a stimulating hormone (recombinant FSH) to stimulate the follicles in your ovary through your IV repeatedly during this 10-hour timeframe. During Day 2 we will collect your urine at specific time points throughout the day. At about 4pm, the visit will conclude.

You will be provided with an additional fecal collection kit to take home before leaving. We will ask you to return this sample to the research coordinator.

Follow-up phone calls: You will be contacted by phone the day after, 3-5 days and 7-10 days after your discharge from the clinic to review any side affects you may be experiencing. If you do experience any side effects, we will contact you and follow these until resolution.

**Optional Experiments on Collected Specimens:**
The researchers would like to save any part of the blood, fecal and urine samples not used up by this study for future research. The choice to let Dr. Polotsky keep the blood, fecal and urine samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your blood, fecal and urine samples can be kept for research, you can change your mind at any time and contact Dr. Polotsky at 303-724-2037 to let him know that you do not want him to use your samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Polotsky decides to destroy them.

In the future, people who do research with your blood, fecal and urine samples may need to know more about your health. While Dr. Polotsky may give them reports about your health, Dr. Polotsky will not give them your name, address, phone number or any other information that will let the researchers know who you are.

The possible benefits of research from your blood, fecal and urine samples include learning more about what causes infertility and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of information from your health records. Dr. Polotsky will protect your records so that your name, address and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any blood or tissue collected and stored by Dr. Polotsky.

Please read each sentence below and think about your choice. After reading each sentence, check “yes” or “no.” If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your blood samples, you may still take part in the study.

I give my permission for my blood to be stored by Dr. Polotsky for future use by the study investigators:

1. I give my permissions for my blood, fecal and urine samples to be kept by Dr. Polotsky for use in future research to learn more about how to prevent, detect, or treat fertility problems related to obesity.

   ☐ Yes ☐ No _____Initials

2. I give my permissions for my blood, fecal and urine samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

   ☐ Yes ☐ No _____Initials

3. I give my permission for my study doctor (or someone he chooses) to contact me in the future to ask me to take part in more research.

   ☐ Yes ☐ No _____Initials

**What are the possible discomforts or risks?**

*Screening blood draw:* can be associated with bruising or bleeding and it involves a brief pricking pain.

*Frequent blood sampling:* can be associated with bruising and bleeding at the site of the IV line. Anemia can result if amounts of blood withdrawn are excessive. You will participate in two 10-hour frequent blood sampling sessions. During these sessions an IV will be placed in a vein in your arm and small amounts of blood (a little less than one teaspoon) will be drawn every ten minutes (about 2 cups of blood to be drawn in the total of two, 10-hour sessions).

*The study drug Cetrorelix:* has been associated with the following side effects: Ovarian Hyperstimulation Syndrome (swollen and painful ovaries) in 3.5% of patients, nausea in 1.3% of patients, and headache in 1.1% of patients. You may also experience redness, bruising, swelling, and/or itching at the site of injection. If you do experience any of these, it is expected to be mild and not last long.

Additional possible risks include delayed menses for up to 1-2 months (occurring in approximately 8-10% of patients) and/or hot flashes. There is also a possibility you could have an allergic reaction to the drug. We will be closely monitoring you throughout the study.

*Recombinant FSH:* has been associated with headache, nausea, fatigue and pelvic pain. There is also a possibility you could have an allergic reaction. Ovarian hyperstimulation (swollen and painful ovaries) has also been associated with increased risk of injury to the ovary.

*Patient confidentiality:* There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

*Pregnancy:* If you become pregnant, the treatment or procedures involved in the study may involve risks to the embryo or fetus which are currently unclear. Before we conduct any study procedures, we will ask you to take a pregnancy test. If you are pregnant, you will not be enrolled in the study. Please use double barrier contraception after the study is completed until you get your first period. Please discuss acceptable contraceptive options with your study doctor.

**What are the possible benefits of the study?**
This study is designed for the researcher to learn more about the relationship between fertility and obesity.

This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the discomforts or risks.

**Who is paying for this study?**
This research is being sponsored by the Eunice Kennedy Shriver Institute for Child Development and Health.

**Will I be paid for being in the study?**
You will be paid $500.00 for completion of the two-day visit. If you leave the study early, or if we have to take you out of the study, you will be paid $20 for each hour of the two day visit you have completed (up to $500). You will also be paid $10 for returning each fecal sample and $25 for all of the urine samples collected. The total compensation possible for the study could be $545.

We are also offering an extra incentive to you; the participant, for being able to do the study visit on 2 weekdays. If are able to do the study visit on 2 weekdays, we will pay you an extra $5 each hour of the two day study visit you have completed (up to $130).

It is important to know that payments for participation in a study are taxable income.

**Will I have to pay for anything?**
It will not cost you anything to be in the study.

**Is my participation voluntary?**
Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

**Can I be removed from this study?**
The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the sponsor may stop the study at any time.

**What happens if I am injured or hurt during the study?**
If you have an injury while you are in this study, you should call Dr. Polotsky immediately. His phone number is 303-724-5276 or 303-724-2001. After hours, the 24-hour emergency service for Dr. Polotsky can be reached by calling 720-848-8000 and asking for the Reproductive Medicine doctor on call.

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

**Who do I call if I have questions?**
The researcher carrying out this study is Dr. Alex Polotsky. You may ask any questions you have now, but if you have questions, concerns, or complaints later, you may call Dr. Polotsky at 303-724-5276 or 303-724-2001. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Dr. Polotsky with questions. You can

also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

You can also talk to a Subject Advocate at the Clinical Translation Research Center (CTRC). The phone number there is 720-848-6662.

**Who will see my research information?**

The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver
- University of Colorado Hospital

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliated hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information, but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Alex Polotsky, MD, MS
Dept of OB/GYN, Mail Stop B198-3
12631 E. 17th Ave.
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- The Eunice Kennedy Shriver National Institute of Child Health & Human Development, who is paying for this research study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator.

**The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make** *all or some* **of the following health information about you collected in this study available to:** The University of Virginia (UVA). Your samples will be sent to UVA to be analyzed; however, none of your identifiable information will accompany the samples.

**Information about you that will be seen, collected, used and disclosed in this study:**

- Name and Demographic Information (age, sex, ethnicity, address, phone number, email address)
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records

**Certificate of Confidentiality**

This study has been issued a Certificate of Confidentiality from the federal government to help protect your privacy. The Certificate prohibits the researchers from disclosing your name, or any identifiable information, document or biospecimen from the research, with the exceptions listed below. A certificate provides protections against disclosing research information in federal, state, or local civil, criminal, administrative, legislative or other proceedings.
These protections apply only to your research records. The protections do not apply to your medical records.
The researchers may disclose your name or identifiable information, document or biospecimen, under the following circumstances:

- To those connected with the research,
- If required by Federal, State or local laws,
- If necessary for your medical treatment, with your consent,
- For other scientific research conducted in compliance with Federal regulations,
- To comply with mandated reporting, such as a possible threat to harm yourself or others, reports of child abuse, and required communicable disease reporting, or
- Under other circumstances with your consent.
- A Certificate of Confidentiality does not protect information you or a member of your family voluntarily release.

**What happens to Data, Blood,Fecal and Urine Samples that are collected in this study?**

Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures of disease. The data and blood collected from you during this study are important to this study and to future research. If you join this study:

- The data, blood, fecal and urine samples given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data and blood collected from you.
- If data, blood, fecal or urine are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

**HIPAA Authorization for Optional Future Experiments**

In this form (section above), you were given the option to agree to additional, optional research experiments (storage of

samples for future research). You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional experiments, as described above.

If you decline to give us permission to use and disclose your information, the samples you provide cannot be used in future experiments, but you can still participate in the main study. Please **initial** next to your choice:

_____ I **give** permission for my information associated with optional future experiments, I have agreed to above, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information associated with the optional future experiments to be used and disclosed.

**Agreement to be in this study and use my data**

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Subject's Name (printed): _____

Signature: _____ Date_____

Consent form explained by:_____ Date_____

Print Name: _____

*If applicable:*

Witness Signature: _____ Date_____

Print Name: _____

Witness of Signature

Witness of consent process