**Title of Study:** Heparin Prophylaxis Dosing for Antepartum Hospitalizations (HEPDOSE)

**NCT Number:** NCT04635839

**Document Date**: October 19, 2021

**Document**: Informed Consent Form

**UNIVERSITY OF CALIFORNIA LOS ANGELES**
**CONSENT TO PARTICIPATE IN RESEARCH**

**Study Title**: Randomized Control Trial of Unfractionated Heparin Dosing for Thromboprophylaxis of Hospitalized Antepartum Patients

## INTRODUCTION

Rashmi Rao, M.D., Thalia Wong, M.D., and associates from the Department of Obstetrics and Gynecology at the University of California, Los Angeles are conducting a research study.

The study doctor and/or study staff will explain this study to you. **Research studies are voluntary and include only people who choose to take part.** Please take your time about deciding whether to participate in this study. Before deciding:

- You can discuss this study with friends and family.
- You can discuss this study with your health care doctor or request a second opinion.
- If you have any questions, you can ask the study doctor or study staff for more information before deciding to participate.

## KEY INFORMATION:

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

**Why am I being invited to take part in a research study?**

We invite you to take part in this research study because you are pregnant and will be admitted to the hospital for at least 72 hours.

**What should I know about a research study?**

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.
- You can discuss this study with friends and family.
- You can also discuss it with your health care doctor request a second opinion.

**Why is this research being done?**

Pregnant patients who are hospitalized for a prolonged period of time are at an increased risk of developing a venous thromboembolism (e.g., a clot in your legs or lung). Because of this increased risk, it is recommended to place pregnant patients who are hospitalized for at least 72 hours on prophylactic anticoagulation (e.g., low dose preventive blood thinner) with unfractionated heparin (e.g., medication to slow the formation of blood clots) to prevent the development of clots. Not enough research has been done to determine the best dosing for unfractionated heparin in pregnancy.

This study is being conducted to investigate the safety and efficacy of two doses of unfractionated heparin that are currently recommended for prophylactic anticoagulation in pregnancy:

1. Standard dose of unfractionated heparin outside of pregnancy
2. Gestational age-based dose of unfractionated heparin (dose of medication depends on the trimester of pregnancy you are in and is higher if you are further along in pregnancy)

Both of these doses are considered "standard of care" or acceptable ways to provide prophylactic anticoagulation in pregnancy. It is thought that changes to your body during pregnancy, including increase in blood volume, greater excretion by the kidneys, and changes in the blood, may require greater amounts of the drug to achieve the same effect. This is why gestational-age based dosing of unfractionated heparin is considered in pregnancy. However, this is not well studied. We want to compare these two doses of unfractionated heparin to evaluate the safest dose for prophylactic anticoagulation of pregnant patients with prolonged hospitalizations.

**How long will the research last and what will I need to do?**
We expect that you will be in this research study from the time you are recruited until you are discharged from the hospital or until you are delivered (if you are admitted for the remainder of your pregnancy).

This will be a randomized control trial, which means all participants will be randomly assigned to one of two groups, like flipping a coin. Women assigned to the first group will receive the standard dose of unfractionated heparin and women assigned to the second group will receive the gestational age-based dose of unfractionated heparin. We ask all participants to be open to being assigned to either group because you will not be able to choose or switch groups.

Unfractionated heparin will be administered to you and you will undergo serial blood draws to monitor the blood clotting parameters while you are receiving the medication. This is part of the "standard of care," meaning if you elect to not participate in the study your medical team will recommend administration of unfractionated heparin at the gestational age-based dosing and you will undergo serial blood draws for monitoring. By being a part of the study, you will receive either the standard dose or the gestational age-based dose of unfractionated heparin and the blood draw results will be collected by the study team. More detailed information about the study procedures can be found under "WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?".

**What kinds of risks or discomforts could I expect?**
Like all medications, unfractionated heparin has the potential to cause side effects. The most common side effects are bleeding or bruising and redness and swelling around the puncture site. Rare side effects include hypersensitivity to the medication and thrombocytopenia. Unfractionated heparin does NOT cross the placenta and is considered safe in pregnancy. Because your medical team will recommend receiving unfractionated heparin as part of standard hospital protocol, participation in this study does not pose an increased risk in exposure to unfractionated heparin. More detailed information about the risks of this study can be found under "WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT? (*Detailed Description*)."

**Are there any benefits if I participate?**
This study may show that standard dosing is effective in preventing blood clots in pregnancy without the increased risk of a higher dose such as bleeding and restrictions on receiving epidurals. If you are randomized into group 1 (standard dosing), then you may directly benefit by receiving the lower dose. Otherwise, you will not directly benefit from participation in this research study. Your participation in this research may help us learn more about the appropriate

dosing of unfractionated heparin for venous thromboembolism prophylaxis, which would benefit future pregnant patients.

**What other choices do I have if I don't want to participate?**
Participation in research is completely voluntary. You can decide to participate or not to participate.

You may wish to talk to your treating physician about your choices before deciding if you will take part in this study. If you decide not to participate in this study, your other choices may include:

- Declining prophylactic anticoagulation and receiving no unfractionated heparin at this time.
- Receiving gestational age-based dosing of unfractionated heparin without being in this study.

Disclosure Statement
Your health care provider may be an investigator of this research protocol, and as an investigator, is interested in both your clinical welfare and in the conduct of this study. You are not under any obligation to participate in any research project offered by your clinician.

**How many people will take part in this study?**
We plan to enroll 46 pregnant patients to take part in this study.

## WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

If you agree to participate in the study:

- Standard lab tests will be performed using your blood sample to make sure that it is safe for you to receive unfractionated heparin and continue in the study.
- You will be randomized into one of the two study groups described below. Randomized means that you are assigned to a group by chance (like a flip of a coin). A computer program will place you in one of the groups. Neither you nor the researchers can choose the group you will be in. You will have an equal chance of being placed in any group.
    - If you are in group 1, you will receive the standard dose of unfractionated heparin.
        - 5,000 units subcutaneous injection every 12 hours (no matter what gestational age)
    - If you are in group 2, you will receive the gestational age-based dose of unfractionated heparin.
        - 1st trimester (less than 14 weeks of gestation): 5,000 units subcutaneous injection every 12 hours
        - 2nd trimester (14-28 weeks of gestation): 7,500 units subcutaneous injection every 12 hours
        - 3rd trimester (greater than 28 weeks of gestation): 10,000 units subcutaneous injection every 12 hours
- You will undergo the following blood draws to monitor the effects of unfractionated heparin. Each collection will be 10 ml of blood (approximately one tablespoon each time). As a reference, about 30 tablespoons of blood are taken at one time when a person donates blood.
    - After the 2nd dose of unfractionated heparin
    - After the 4th dose of unfractionated heparin

    - After the 10th dose of unfractionated heparin
    - Every 7 days after the 10th dose of unfractionated heparin
- The lab tests performed on the collected blood samples are standard of care and are required to monitor you while receiving unfractionated heparin. The results of the tests will be provided to you.
- If the blood draw measurements demonstrate that your coagulation level is elevated, the study team will decrease the dose of unfractionated heparin or hold the medication per the study protocol to ensure safety.
- After the 10th dose of unfractionated heparin and then every 7 days while you are receiving the medication, the study team will formally ask you if you are experiencing any side effects from the medication.
- The study team will collect information from your medical records. Examples include your age, sex, race/ethnicity, details of your labor and delivery course, and overall health in your pregnancy.

## WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT? (Detailed Description)

**Risks of Medication**

Unfractionated heparin has the potential to cause side effects. The most common side effects are bleeding or bruising and redness and swelling around the puncture site. Rare side effects include hypersensitivity to the medication (hives, fever, swelling of throat, difficulty breathing) and thrombocytopenia. If significant side effects occur, the medication will be discontinued. Unfractionated heparin does not cross the placenta and is considered safe in pregnancy without any increased risk of fetal malformation. Unfractionated heparin is administered as a subcutaneous injection, which means an injection under the skin, and may cause temporary pain after administration. Because your medical team will recommend administration of unfractionated heparin as part of standard hospital protocol for prophylactic anticoagulation, participation in the study does not pose an increased risk in exposure to unfractionated heparin.

Currently both standard dose and gestational age-based dose of unfractionated heparin are recommended for prophylactic anticoagulation of hospitalized antepartum patients. Because standard dosing is lower than gestational age-based dosing, it might be less effective in preventing blood clots. However, the overall risk of developing a blood clot is very low (less than 2%), and standard dosing is the dose recommended outside of pregnancy. Gestational age-based dosing is higher and theoretically may limit your ability to receive an epidural. However, we will be monitoring you closely with serial blood samples and decrease the dose if the lab results are elevated in order to decrease this risk. At UCLA, the gestational age-based (higher) dosing is the current standard of care because of the theoretical changes in pregnancy that may result in requiring greater amounts of heparin to achieve the same effect. If you are not in the study, your medical team will recommend gestational age-based dosing as part of standard hospital protocol for prophylactic anticoagulation, so those assigned to group 2 are not exposed to an increased risk.

There may be risks associated with the drug/treatment that are as yet unknown, but that the researcher will advise you if any new information becomes available that might affect your desire to participate in the study.

**Risks of Study Procedures**

Possible side effects from blood draws include temporary discomfort from the needle stick, bruising and, rarely, infection and fainting.

**Risks Associated with Randomization**
You will be assigned to a study group at random (by chance). Your assignment is based on chance (like a coin flip) rather than a medical decision made by researchers. The study group you are assigned to might not be the group you would before to be in. It might also prove to be less effective or have more side effects than the other study group, or standard treatments available for your condition.

## HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?

The study doctor and study staff will do their best to make sure your private information is kept confidential. Any information that is obtained in connection with this study and that can identify you will be handled as confidentially as possible. All identifiable information about you will be replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data and only available to the research team. All research data and records will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security.

The research team, authorized UCLA personnel, the study sponsor (remove if not applicable), and regulatory agencies such as the Food and Drug Administration (FDA), may have access to study data and records to monitor the study. Research records provided to authorized, non-UCLA personnel will not contain identifiable information about you. Publications and/or presentations that result from this study will not identify you by name.

Employees of the University may have access to identifiable information as part of routine processing of your information, such as lab work or processing payment. However, University employees are bound by strict rules of confidentiality.

Because this study involves the treatment of a medical condition and/or medical procedures, a copy of this consent form will be placed in your medical record. This will allow the doctors that are caring for you to obtain information about what medications and/or procedures you are receiving in the study and treat you appropriately.

## USE OF DATA AND SPECIMENS FOR FUTURE RESEARCH

The researchers intend to keep the research data and records indefinitely for future research. Your data, including coded data, may be kept for use in future research, but will not be shared outside the study team.

## ARE THERE ANY COSTS FOR TAKING PART IN THIS STUDY?

There will be no additional cost to you or your health plan as a result of your participation in this study. Items and services described in this consent form would have occurred regardless of your participation in this study or, if research-related, will be provided to you at no cost.

## WILL I BE PAID FOR MY PARTICIPTION?

You will not be paid for your participation in this research study. You will not be reimbursed for any out-of-pocket expenses, such as parking or transportation fees.

## WHAT OTHER THINGS SHOULD I CONSIDER BEFORE PARTICIPATION?

**Use of Specimens:**

Any specimens (e.g., tissue, blood, urine) obtained for routine lab testing will be discarded or destroyed once they have been used for the purposes described in the protocol.

## WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

**The Research Team:**
If you have any questions or concerns about the research or your participation in this study, please contact:

Rashmi Rao, MD – Principal Investigator
Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine
10833 Le Conte Ave.
Los Angeles, CA 90095
Phone: 310-794-7274

Thalia Wong, MD – Co-Investigator
Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine
10833 Le Conte Ave.
Los Angeles, CA 90095
Phone: 310-210-2246

**UCLA Office of the Human Research Protection Program (OHRPP):**
If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, you may contact the UCLA OHRPP through the following:

Phone: (310)206-2040
E-mail: participants@research.ucla.edu
U.S. mail: UCLA OHRPP, Box 951406, Los Angeles, CA 90095-1406

**Public Information about this Study:**
*ClinicalTrials.gov* is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

## WHAT HAPPENS IF I BELIEVE I AM INJURED BECAUSE I TOOK PART IN THE STUDY?

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number(s) listed above.

If you are injured as a result of being in this study, UCLA will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor [sponsor name], or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call the UCLA Office of the Human Research Protection Program at 310-206-2040 or send an email to participants@research.ucla.edu.

## WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You can choose whether or not you want to participate. Whatever decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the medical care you receive from UCLA.
- If you decide to take part, you can leave the study at any time.
- If you decide to stop being in this study you should notify the research team right away. The researchers may ask you to complete some procedures in order to protect your safety.
- If you decide not to take part, you can still receive medical care from UCLA.

## HOW DO I INDICATE MY AGREEMENT TO PARTICIPATE?

If you agree to participate in this study you should sign and date below. You have been given a copy of this consent form and the Research Participant's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

### SIGNATURE OF THE PARTICIPANT

_____
Name of Participant

_____ _____
Signature of Participant Date

### SIGNATURE OF PERSON OBTAINING CONSENT

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date