Principal Investigator: Shanlee Davis, MD
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Study Title: Body Composition in Infants with Klinefelter Syndrome and Effects of Testosterone Treatment

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You have been asked to decide for your child whether he should 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 don't understand before deciding whether or not to take part.

Why is this study being done?

This study plans to learn more about the amount of muscle and fat (body composition), motor development, and male hormones in infant boys with Klinefelter syndrome (47,XXY). We know that older boys and men with Klinefelter syndrome have more fat compared to muscle, but we do not know if this is true at birth or develops over time. We also want to know if muscle mass plays a role in development of motor skills. Finally, we would like to learn how the male hormone testosterone changes the amount of muscle and fat and motor skills development.

Your child is being asked to be in this research study because he is an infant with a diagnosis of Klinefelter syndrome (karyotype 47,XXY).

Other people in this study

Up to 20 people from your area will participate in the study.

What happens if my child joins this study?

If your child joins the study, he will have the first study visit between 6-15 weeks of age. At the end of that visit, half of the children will be assigned to get a testosterone shot once a month for 3 months while the other half will not receive testosterone. At the end of the three months, the final study visit will take place for all participants, whether or not they received the shots. The total length of the study is about 3 months.

<u>The first visit and last visits will occur at Children's Hospital Colorado and include</u>:

- You answering some questions about your child
- a physical exam of your child including measurements of your child's body and penis
- a play-based exam of how your child's muscles work
- measurement of the amount of muscle and fat by a type of scale called the PEA POD

- blood draw (first visit only) to test levels of hormones in the blood
- urine collected by a bag (first visit only) to test levels of hormones in the urine

In between the first and last visits:

- Half of children will receive a total of 3 testosterone shots, while the other half of the children will not receive any shots.
- If your child is in the group to receive shots, he will get a shot in his thigh once a month for three months, starting with the first visit.
- All parents will get two calls from a research team member to check in during the study. The first will be one week after their initial visit and the second about a month later.

Week	Study Activity	Which subjects
1	Baseline study visit • Consent • History • Physical Examination • Play-based developmental evaluation • PEA POD measurement • Blood and urine collection • Randomization to treatment or not	All
1	Testosterone injection #1	Treatment group only
2	Phone call to parents	All
4	Testosterone injection #2	Treatment group only
5	Phone call to parents	All
8	Testosterone injection #3	Treatment group only
10-12	Final study visit • History • Physical Examination • Play-based developmental evaluation • PEA POD measurement	All

How we decide which study group you will be in

This study will have 2 different groups of infants, one group will receive testosterone shots and the other will not. You cannot choose which group your child will be in. To decide which group your child will be in, we will use a method of chance. This method is like flipping a coin or rolling dice. We will open an envelope together at the end of the first study visit that tells us which group he will be in.

You will know what study group your child is in, but not all the study team will

You will know what study group your child is in. Dr. Davis will also know, but all of the other study team members will not know. This information needs to be kept secret so that the study results are based on scientific findings, not peoples' opinions. We will ask you not to tell any of the other people on the study team about which group your child is in.

What are the possible discomforts or risks?

Part of the physical exam and PEA POD measurement will require all clothes to be removed. This could cause your baby to be uncomfortable but should not cause pain. The test itself takes about a minute and we usually do it twice. There are no known risks with the PEA POD.

In this study we will need to get about 2 teaspoons of blood from your child. We will get blood by putting a needle into one of his veins and letting the blood flow into a glass tube. He may feel some pain when the needle goes into the vein. A day or two later, your child may have a small bruise where the needle went under the skin.

The testosterone shots are given into the muscle in your child's thigh. A day or two later, your child may have a small bruise, swelling, or redness of the area where the needle went under the skin. Skin rashes near where the needle went in or pimples on the infants face can happen sometimes. The testosterone may make your child's penis grow and could cause him to have erections. Rare side effects of testosterone, such as blood clots, difficulty clotting, increased red blood cells, and anaphylaxis or allergic reaction have not been reported with the low doses we are using in this study, however may be possible. It is also possible that testosterone shots have other risks that are unknown at this time.

The play-based exam of your child's muscles and development may show abnormalities. If your child is found to have abnormalities on this test we may recommend further evaluation for your child. This may be distressful to you as the parents. Any additional evaluation would be your decision as the parents and would not be required of the study.

There is a risk that people outside of the research team will see your child's research information. We will do all that we can to protect this information, but it cannot be guaranteed.

The study may include risks that are unknown at this time.

What are the possible benefits of the study?

This study is designed for us to learn more about how testosterone affects infants with Klinefelter syndrome. We are looking at the amount of muscle and fat, and at your baby's motor skills. However, there is no guarantee that your child's health will improve if you join this study. Also, there could be risks to being in this study. These risks are described in the section describing the discomforts or risks.

Are there alternative treatments?

Testosterone shots are currently only recommended for infants with a small penis (called micropenis). Infants with micropenis can get testosterone shots in the same dose we are giving in this study. If your child has micropenis, but is not chosen to be in

the study group that receives testosterone shots, you can still choose to do these shots after the study is completed. If your child does not have micropenis, there are not alternative medical treatments for infants with Klinefelter syndrome. Your child may continue to receive any therapies or other treatment prescribed by his primary doctor during the study, just not testosterone or testosterone-related products.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to have your child take part in this study. Your child may leave this study and still have these other choices available.

Who is paying for this study?

This research is being paid for by a grant from the Colorado Clinical and Translational Science Institute.

Will my child be paid for being in the study?

You/your child will be paid $20 for the first and last visit of this study. This will add up to a total of $40 if your child completes both of the visits. If your child leaves the study early, or if we have to take your child out of the study, you will be paid only for the visits completed.

If you live more than 100 miles from Children's Hospital Colorado, some travel expenses (hotel stay or mileage reimbursement) may be eligible for reimbursement up to a maximum of $100.

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

Will I have to pay for anything?

It will not cost you anything to be in this study. You will not have to pay for any medical care that is part of this study, including tests and the study drug. You or your insurance company will have to pay for other medical expenses that occur during the time your child is in the study, including diagnosis and treatment of any complications.

Is my child's participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to have your child take part in this study. If you choose to have your child take part, you have the right to stop at any time. If you refuse or decide to withdraw later, your child will not lose any benefits or rights to which he is entitled.

If your child leaves this study, he will still receive normal medical care. The only medical care that your child will lose is the medical care he is getting as part of this study. Your child might be able to get that same kind of medical care outside of the study. Ask your study doctor.

If there are any new findings during the study that may affect whether you want your child to continue to take part, you will be told about them.

Can my child be removed from this study?

The study doctor may decide to stop your child's participation without your permission if the study doctor thinks that being in the study may cause your child harm, or for any other reason.

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. Davis immediately. Her phone number is 720-777-6073.

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. Shanlee Davis. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Davis at 720-777-6073. 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. Davis with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

You may also contact a Research Advocate at the Clinical Translational Research Center. The number there is 720-848-6662.

A description of this clinical trial will be available on http://www.Clinical 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 this Web site at any time.

Who will see my research information?

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

- University of Colorado Denver

- Children's Hospital Colorado (CHCO)

CHCO shares a medical record system with the Barbara Davis Center and PedsConnect; therefore it is also possible that your child's information could be viewed by healthcare professionals at these organizations.

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

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

We will do everything we can to maintain the confidentiality of your child's 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 child's 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 child's part in this study will end and no further information about your child will be collected. Your cancellation would not affect information already collected in this study.

Shanlee Davis, MD
Children's Hospital Colorado
13123 East 16th Ave B265
Aurora, CO 80045

Both the research records that identify your child 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.
- 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 your child, private.

You have the right to request access to your child's personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study is completed.

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 some of the following health information about you collected in this study available to:

- Le Laboratoire de Biologie Hormonale (blood samples only)
- The laboratory of Dr. Nanette Santoro at the University of Colorado Denver

Inclusion in the research study involves the use of your child's genetic information (Klinefelter syndrome). Your child's genetic information will be known by the members of the study team.

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

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

What happens to data, blood, and urine 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, blood and urine specimens collected from your child during this study are important to this study and to future research. If your child joins this study:

- The data, blood, or urine specimens given by your child to the investigators for this research no longer belong to you or your child.
- Both the investigators and any sponsor of this research may study your data, blood, or urine specimens collected from your child.
- If data, blood, or urine specimens are in a form that identifies your child, 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 or your child.
- There is no plan for you or your child to receive any financial benefit from the creation, use or sale of such a product or idea.

Agreement to be in this study and use my child's 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 child's information as stated in this form. I know that being in this study is voluntary. I choose to have my child be in this study: I will get a signed and dated copy of this consent form.

Child's Name: _____

Parent's Signature:_____ Date:_____

Print Name:_____

Consent form explained by:_____ Date:_____

Print Name: _____

Witness Signature: _____ Date_____
(if applicable)

Print Name: _____

Witness of Signature ☐

Witness of consent process ☐

Investigator: _____ Date: _____
Investigator must sign within 30 days