

Principal Investigator: Shanlee Davis, MD, MSCS
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TESTO: Testosterone Effects on Short-Term Outcomes in Infants with XXY

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 infant boys with XXY (Klinefelter syndrome). We want to know how the male hormone testosterone changes body fat, development, and other hormones in the body. We know that some boys with XXY have higher body fat or delays in development. Some people think that testosterone in infancy may be helpful, but this has not been fully studied.

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

Other people in this study

Up to 75 people will participate in the study.

What happens if my child joins this study?

This study is 6 months long. There will be a total of 3 study visits every 3 months.

During the study, your child will get the study drug, testosterone. Your child will get one shot in his thigh muscle every month for a total of 6 shots. 3 shots will be testosterone and 3 will be placebo. A placebo is a liquid that looks like medicine but is not real. It will have no medical effect on your child. This will allow us to see what changes happen when he is not getting testosterone.

There are two groups in the study. Half of the boys will get the testosterone shots in the first 3 months of the study and the other half will get testosterone in the last 3 months. You cannot choose what group your child will be in. You will have the option to come in to the clinic for the shots or learn how to do them at home. If you do them at home, you will keep the medication at room temperature and complete a log when the shot is given.

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CF-151.S, Effective 7-19-13

Timeline of study activities		
Study Week	Study Activity	Location
1	Study visit #1 and shot #1	Children's Hospital Colorado (CHCO)
4	Shot #2	<i>Home or CHCO</i>
8	Shot #3	<i>Home or CHCO</i>
12	Study visit #2 and shot #4	Children's Hospital Colorado (CHCO)
16	Shot #5	<i>Home or CHCO</i>
20	Shot #6	<i>Home or CHCO</i>
24	Study visit #3	Children's Hospital Colorado (CHCO)

At each study visit your child will have a:

- Physical exam including body measurements
- Play-based evaluation of his developmental skills
- Measurement of the amount of body fat by a type of scale called the PEA POD
- Blood draw
- Collection of urine and stool

We will also ask you to:

- Answer some questions about your child and his medical history
- Keep track of when the shots are given and who gives them
- Let the study team know immediately of any possible side effects

We will video-record you while completing some of the study assessments. The video recording(s) will include a code number and will be treated like other data collected in the study. The recording(s) will be reviewed by study staff in order to score the assessments. We will also take a photo of you for our research records.

How we decide which study group your son will be in

This study will have 2 different groups of infants. You cannot choose which group your son 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.

You will not know which group your son is in

You will not know what group your son is in. Neither will your study doctor. This information needs to be kept secret so that the study is based on scientific results, not on peoples' opinions.

At the end of the whole study we will tell parents what group their son was in. If your son is in an emergency, make sure you tell the emergency staff about this study. They can contact us and we will give them all relevant information.

What are the possible discomforts or risks?

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CF-151.S, Effective 7-19-13

Part of the physical exam and PEA POD measurement will require all clothes to be removed. This could cause your son to be uncomfortable but should not cause pain. The test itself takes 1-2 minutes 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 son at each of the visits. 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, he may have a small bruise where the needle went under the skin.

The shots are given into the muscle in your son's thigh, which may be painful. A day or two later, your son may have a small bruise, swelling, or redness of the area where the needle went under the skin. Infection under the skin where the shot was given is possible. The testosterone may make your child's penis grow and may cause him to have erections. It may also cause pimples or increased hair growth. Rare side effects of testosterone, such as blood clots, difficulty clotting, increased red blood cells, severe allergic reaction, and advancement in growth and puberty have not been reported with the low doses we are using in this study, however may be possible. We do not know if testosterone in infancy alters fertility later in life. It is also possible that testosterone shots have risks that are unknown at this time.

The play-based exam of your son's developmental skills may show delays in development. If your child is found to have delays on this test we may recommend further evaluation for your child. This may be stressful to you as the parents. Any additional evaluation or treatment would be your decision as 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 XXY. One study has suggested testosterone may have benefits on neurodevelopmental outcomes in XXY, however, there is no clear consensus on the benefit. 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?

There may be other ways of treating risks in XXY. These other ways include early intervention therapies (i.e. physical, occupational, and behavioral therapies), healthy diet,

and regular exercise. These alternative treatments can still be used if you are in this study. You could also choose no treatment at all.

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

You can get the study drug from other places

If you were not in this study, you could buy testosterone at a pharmacy with a prescription from your son's doctor. Testosterone is approved by the FDA but not for the way in which it is used in this study. This is called off label use. You or your insurance company would have to pay for the study drug.

Who is paying for this study?

This research is being paid for by the National Institute of Child Health and Human Development.

Will I be paid for being in the study?

You will not be paid to be in the study. You may have access to clinical care in the eXtraordinary Kids Clinic earlier or more often than if you are not in the study.

If you live more than 100 miles from Children's Hospital Colorado, some travel expenses can be reimbursed. These include one night in a hotel and one economy class airline ticket per study visit. There are reimbursement limitations.

Reimbursements are not subject to IRS regulations and will not be reported as 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 or additional evaluations you choose to do outside of the study.

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 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?

Your son may be taken out of the study if the study doctor thinks it is not safe for you to be in the study. You can be taken out of the study even if you do not want to leave the study. Also, the sponsor can decide to stop the study at any time.

What happens if your child is injured or hurt during the study?

If your son has 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.

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.

Things that must be reported to the authorities

We respect your right to privacy. But there are some things we cannot keep private. If you give us information about child neglect or child abuse, we have to report that to Social Services. If you give us information about someone hurting someone else, we have to report that to the police. If a court orders us to hand over your study records, we have to hand them over to the court.

Genetic Information Nondiscrimination Act (GINA)

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009. Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Use of Video for Teaching Purposes

The investigators may want to use the videos collected for research to train other clinicians and scientists on testing procedures. This is not required in order to be a part of the study. Your face might be seen and information about your condition might be shared, but your full name and information will not be shared with those being taught using the collected videos. We cannot guarantee the video will be deleted after the study is completed. If you are not comfortable with the use of your videos for teaching, you may choose below to allow or not allow.

Please initial your choice regarding use of videos collected for research used for teaching.

____ I agree to allow these videos collected for research to be used for teaching purposes.

____ I do not agree for these videos to be used for teaching purposes.

Storage of data, blood, urine and stool for this study or for banking for future use

I give my permission for my child's data, blood, urine and stool to be stored in a bank at the University of Colorado for future use. This may include future genetic studies. If you change your mind, contact Dr. Davis and she will have the samples removed.

1. I give my permission for my child's blood, urine, and stool samples to be kept by Dr. Davis for use in future research to learn more about how to prevent, detect, or treat X&Y chromosome variations.

_____ YES _____ NO _____ Initials

2. I give my permission for my child's blood, urine, and stool samples to be used by Dr. Davis or someone she chooses for research about other health problems (for example: causes of low testosterone, heart disease, osteoporosis, diabetes).

_____ YES _____ NO _____ Initials

Being placed on a recruitment list for future studies

We may be doing other studies in the future, and would like to make a list of people who are interested in doing more studies. If you decide now that we can keep your child's name on a list, you can change your mind anytime. If you change your mind, contact Dr. Shanlee Davis and she will remove your name from the list.

I would like to be included on a list of people who may be contacted about future studies. _____ Initials

I would not like to be included on a list of people who may be contacted about future studies. _____ Initials

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.ClinicalTrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At

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CF-151.S, Effective 7-19-13

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

Who will see my research information?

The University of Colorado Denver (UCD) and its affiliated hospitals 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, MSCS
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)

Combined Biomedical Consent and Separate Main and Optional HIPAA authorizations
CF-151.S, Effective 7-19-13

- 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.

Some of the research procedures involve genetic testing or the use of your genetic information. Your genetic information will not be released to others outside of the study.

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 record that are relevant to this study, including but not limited to diagnoses, history and physical, laboratory studies, radiology studies, procedure results
- Research visit and research test records
- Blood, urine, and stool samples and the data with the samples

What happens to data, blood, urine, and stool 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, urine, and stool 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, or blood, urine, and stool collected from your child.
- If data and blood, urine, and stool 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.

HIPAA Authorization for Optional Additional Study Procedures

In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures as described above.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:

_____ I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

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