INFORMATION FOR PARTICIPANTS

Detection of Testosterone Microdosing in Women

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Project Sponsor: This study was designed by the investigators to improve detection of testosterone doping. It is intended for funding by the Partnership for Clean Competition, the major US public sector anti-doping agency.
The study is sponsored by the Sydney Local Health District (SLHD). The manufacturer of the testosterone gel has no relationship with the study other than providing the product for purchase by the SLHD.

INTRODUCTION:

You are invited to take part in a research study into new ways to detect the use of low doses of testosterone for doping in women.

The lure of fame and fortune through competitive success in elite sports will always tempt some athletes to cheat including by doping using performance enhancing drugs.
At present, testosterone is known to be used illegally to enhance athletic performance. Testosterone is the most powerful and widely used drug in doping to gain unfair advantages in athletic performance. Anti-doping detection tests, based on urine samples are used to detect, deter and penalise cheating athletes who use testosterone in elite athletics or training.
However, it is not clear how quickly these tests detect testosterone, especially for women, and there is a concern that low doses of testosterone may be missed by the standard urine tests. This study is designed to address this important gap in knowledge in anti-doping science as well as aiming to develop better, more accurate tests. This study is for the first time studying in detail the use of blood tests to see how well they add to and improve on the standard urine tests to detect use of testosterone.

This Participant Information Sheet will tell you about what is involved in the study and help you decide whether you wish to take part. You are not obliged to take part in this study.

Please read this information carefully. If there is anything you do not understand or if you feel you need more information about anything, please ask. Before you decide, please feel free to talk things over with a relative, a friend or your own doctor. If you do agree to take part in the study, you will be asked to sign the consent form to confirm that you understand the requirements of the study and are willing to participate fully in the study.

WHY HAVE I BEEN ASKED TO TAKE PART?

You have been invited to take part in this research because you are a healthy woman of suitable age willing to participate in this research study which is designed to improve scientific knowledge but is not intended to improve your health.

The study aims to include 12 women, aged 18 to 60 years of age and in good health and who are not pregnant or breast feeding.

BACKGROUND:

Standard urine testing is now able to detect most artificial androgens for long periods after the last dose. As a result, efforts by those intending to cheat in sports have been directed to using low dose testosterone in an attempt to evade detection. So, the sensitivity of the urine detection methods needs to be fully evaluated and improved. This study is therefore aiming to do so by investigating whether adding blood tests can improve the sensitivity of tests to detect low dose testosterone use in female athletes.

WHAT IS THE PURPOSE OF THIS RESEARCH?

AIM:

The aim of this study is to determine (a) how responsive and effective are the standard urine detection tests for administration of low doses of testosterone in women and (b) whether the addition of blood tests can improve the overall responsiveness to detect testosterone administration.

The study has three periods – at least two weeks of "before treatment", one week of daily treatment and three weeks of "after treatment". So, if you are eligible and provide written consent, the study will require you to make 12 visits to the clinic over 6 weeks and at each visit you will be required to supply a blood and a urine sample.

During the two or more weeks of "before treatment" period, you would be required to attend the clinic on 6 occasions (including the visit V6 on the first day of

treatment) over at least two weeks to establish your usual baseline levels of the hormones measured in the anti-doping tests.

During the treatment period of 1 week you will be applying a dose of the testosterone gel to your skin from a pump pack (like a suntan lotion spray) each day for 1 week. The dose to be used will be one actuation of the pump pack which will provide one dose of the gel containing 12.5mg testosterone to be applied on your skin each day. During the treatment period you would need to attend the clinic at the end of the 1st week to provide blood and urine samples.

We will supply the testosterone gel pump and we will give instructions how to use it. You should apply the testosterone gel after a morning shower, cover the area with clothes, wash your hands thoroughly afterwards. Gel treated area should not be in contact with another person's skin until after washing your hands and for at least 6 hours to avoid transferring any gel to them. You should not bathe, swim or shower again for at least 6 hours to allow the gel to absorb.

During the "after treatment" period we need to study how quickly the testosterone disappears from the body by checking 5 more sets of blood and urine samples over 3 weeks.

Please see the attached flow chart for a schedule of all visits and tests.

CAN I WITHDRAW FROM THE STUDY?

Taking part in this medical research is entirely voluntary. If you do decide to take part, you can withdraw at any time without having to give a reason.

WHAT WILL HAPPEN TO ME IF I TAKE PART?

Please see attached schedule

The first visit (Screening, V1)

- You will be asked whether you have any medical conditions or are on any medicines that may prevent you from entering this study also if you are pregnant, planning pregnancy or breast feeding within next 6 months.
- You will be asked to read and sign a consent form prior to your entry into this study.
- Your medical history will be taken and will include the date of the last menstrual period/menopausal status, marital and fertility/contraception status (including oral or implantable contraceptives or hormones), smoking and alcohol usage
- Your height, weight, pulse and blood pressure will be measured.
- A blood sample will be taken from a vein in your arm to check your blood count, liver and kidney function, your hormone levels (this includes a sample

to be tested at the end of the study) and DNA (to determine genetic reasons that influence testosterone excretion or activity in the body). In total approximately 35 mls of blood will be taken.
- A urine sample.
- This first visit should take about 30 minutes.

Visit 2 - 5

- These visits will be spread over at least 2 weeks after the 1st visit
- A blood sample of about 10 ml will be taken to be stored for hormone analysis at the completion of the study.
- A urine sample will be taken.
- These visits will take about 15 minutes.

Visit 6

- This visit will be at least two weeks after the 1st visit
- A blood and urine sample will be taken
- You will be provided with the testosterone gel bottle for the treatment
- You will be required to apply the testosterone gel according to the instructions which will be provided to you. You will use one activation of the pump daily for one week
- This first visit should take about 30 minutes.

Visit 7

- This visit will be at the end of the week of treatment period
- You will bring back the treatment bottle and return it to the clinic
- You will provide a blood and urine sample
- This visit should take about 30 minutes.

Visits 8-12

- These visits will be over the first two weeks after the end of treatment
- They will be at 8,9,11,14 and 21 days after the end of treatment
- At each visit you will provide a blood and urine sample
- These visits will take about 15 minutes.

Please see the study schedule for the duration of the study, the number of visits and what is required for each day of the study.

WHAT WILL HAPPEN TO MY SAMPLES

Samples will be sent to USA accredited laboratory as facilities for certain testing are not available in Australia. Your privacy will be protected by coding the samples with a unique identification code. This code can only be re-identified by Concord hospital researches. No personal information will be sent with your samples.

Unused samples after the testing has been undertaken will be stored in the Andrology Department Concord Hospital for future use associated with this study.

COSTS

Participation in this study will not cost you anything and the study drug (testosterone gel in a pump pack) will be supplied to you without charge.

You will be paid for the time and travel costs of attending the clinic after completing the study. If you complete the study fully, you will receive payment ($250) based on full participation. As your contribution to the study depends on availability of all the data, incomplete participation will mean your data cannot be used for this study's purpose. Payment for incomplete participation will be pro-rated according to the number of visits attended based on payment rate for incomplete participation ($100).

WHAT DO I HAVE TO DO?

There are no life style restrictions as part of this research. You are not required to be fasting before any tests but it is best if you can visit the clinic at similar times of day.

At the end of the treatment period, you must attend the scheduled visit without taking testosterone on the day of that clinic visit.

Please inform the research staff if you have had any change in your health or medications during the study.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

While we intend that this research study furthers knowledge in anti-doping science, it will not be of direct benefit to you.

All the screening and safety blood tests (biochemistry, hematology) will be made available to you. If there is an unexpected abnormality, this will be explained to you and you will be advised to discuss this with your specialist or general practitioner.

WHAT ARE THE RISKS OF TAKING PART?

Medical treatments may cause side-effects. We expect no serious side-effects from this short period of testosterone treatment.

You may have all, some or none of the side-effects listed below and they may be mild, moderate or severe. If you have any of these side-effects or you are worried about them, please talk to your study investigator. They will also be looking out for any side-effects and will discuss with you the best way of managing any that do occur.

Many side-effects go away shortly after treatment ends. However, some can be serious, long-lasting or permanent.

Side effects:

- Pain and minor bruising from having blood taken is rare and the risk is minimised by having very experienced nursing staff do these procedures.
- Fainting whilst having blood taken is rare, occurring in much fewer than 1% of people having these procedures. If you have fainted in the past, please let the nursing staff know in advance so you may have these procedures lying down on a bed.
- Transfer of the testosterone to a partner or child may occur if the gel on your skin directly contacts another person's skin. To prevent this, you should apply the testosterone gel to the body as directed after your morning shower and cover the area with clothes. You should not have direct skin contact of the treated area with another person for at least 6 hours after applying the gel to your skin.

For women, testosterone administration at sufficiently high doses and for long enough could cause development of acne, excessive hair growth, voice change (deepening) and clitoral enlargement. Also because of alcohol this medication contains, frequent applications to the skin may cause irritation and skin dryness. These changes usually take many weeks to months to develop at higher doses and higher frequency than are to be used in this study. In the unlikely event that any such changes start to occur during your week of treatment, you should immediately notify the study investigator and stop the treatment. These changes are reversible and will disappear a few weeks after ceasing the treatment.
Testosterone gel will not stain your clothing.

WHAT IF NEW INFORMATION BECOMES AVAILABLE?

Sometimes during a study new information becomes available about the treatment that is being studied. This is mostly the case with new medication and is not likely to be the case for an old drug like testosterone. While you are participating in the study you will be kept informed of any significant new findings that may affect your health or willingness to continue in the study.

CONFIDENTIALITY

Research data will be kept in the Department of Andrology at Concord Hospital for 15 years. Electronic information will be stored on a password protected hospital computer and paper copies of the files will be stored in a lockable filling cabinets in the Andrology Department that only researches can access.
If you consent to take part in this study your research records may be inspected by the researchers, by regulatory authorities or by the Human Research Ethics Committee. By signing the consent form you are giving permission for this to be done. All details obtained by those named will remain confidential. A report of this study may be submitted for publication but individual participants will not be identifiable.

COMPENSATION

Every reasonable precaution will be taken to ensure your safety during the study. If you suffer any injury as a direct result of participating in this research project, hospital care and treatment will be provided at no extra cost to you.

FURTHER INFORMATION

When you have read this information, ... will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact the Research Nurse on 9767 7222. This information sheet is for you to keep.

This study has been approved by the SLHD Human Research Ethics Committee of Concord Hospital. If you have any concerns or complaints about the conduct of the research study, you may contact the Ethics Committee, on 9767 6522.

Visit	V1	V2,3,4,5	V6	V7	V8	V9	V10	V11	V12
Study Phase	before treatment		Treatment		after treatment				
Day	-14	-13 to -1	0	7	8	9	11	14	21
Screening,eligibility&consent	x								
Treatment			Supply	Return					
Blood sample	x	xxxx	x	x	x	x	x	x	x
Blood sample for DNA	x								
Urine sample	x	xxxx	x	x	x	x	x	x	x
Safety: clinical				x				x	x
Safety: bloods	x			x					x

Visit	Date	Time
Screening Visit 1		
Visit 2		
Visit 3		
Visit 4		
Visit 5		
Visit 6		
Visit 7		
Visit 8		
Visit 9		
Visit 10		
Visit 11		
Visit 12		

Please keep this as your record of appointments

1 One dose (12.5mg) of testosterone gel (Testogel) will be applied to the skin each day for 7 days
2 Blood samples from a vein in your arm and a urine test will be obtained on every clinic visit

CONCORD
REPATRIATION GENERAL
HOSPITAL

NSW GOVERNMENT Health
Sydney
Local Health District

Detection of Testosterone Microdosing in Women

PARTICIPANT CONSENT FORM

I, ...[name]

of.....[address]

have read and understood the Information for Participants for the above named research study and have discussed the study with .....
.....

- I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications as far as they are currently known by the researchers.

- I understand that, during the course of this study, my research records may be accessed by the researchers, by regulatory authorities or by the Ethics Committee approving the research in order to verify results and determine that the study is being carried out correctly.

- I freely choose to participate in this study and understand that I can withdraw at any time.

- I also understand that the research study is strictly confidential.

- I hereby agree to participate in this research study.

Name (Please Print):.....

Signature:..... **Date:** .....

Name of Person who conducted informed consent discussion (Please Print):

.....

Signature of Person who conducted informed consent discussion:

.....

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