



ANDROGEN DEFICIENCY

A GUIDE TO MALE HORMONES

A BOOKLET IN THE SERIES
OF CONSUMER GUIDES
ON MALE REPRODUCTIVE
HEALTH FROM



ANDROLOGY AUSTRALIA

What every man needs to know

First published in July 2003
by Andrology Australia

5th Edition, December 2015

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Health information in this booklet describes ANDROGEN DEFICIENCY. Diagnosis and treatment options are described to help men and their families understand the health problem, make men aware of the available treatment options, and to help make talking with their doctor easier.

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Andrology Australia (The Australian Centre of Excellence in Male Reproductive Health) is supported by funding from the Australian Government Department of Health, and is administered by Monash University.

AT A GLANCE

What is testosterone?

Testosterone is the most important androgen (male sex hormone) in men and it is needed for normal reproductive and sexual function. Testosterone is important for the physical changes that happen during male puberty, such as development of the penis and testes, and for the features typical of adult men such as facial and body hair. Testosterone also acts on cells in the testes to make sperm.

Testosterone is also important for overall good health. It helps the growth of bones and muscles, and affects mood and libido (sex drive). Some testosterone is changed into oestradiol, the female sex hormone, and this is important for bone health in men.

What is androgen deficiency?

Androgen, or testosterone, deficiency is when the body is not able to make enough testosterone for the body to function normally. Although not a life-threatening problem, androgen deficiency can affect your quality of life.

What are the symptoms of androgen deficiency?

Symptoms of androgen deficiency include low energy levels, mood swings, irritability, poor concentration, reduced muscle strength and low libido (sex drive). Symptoms often overlap with those of other illnesses. Androgen deficiency has different symptoms depending on the age of the man.

What causes androgen deficiency?

Androgen deficiency can be caused by genetic disorders, medical problems, or damage to the testes or pituitary gland. Androgen deficiency happens when there are problems within the testes or with hormone production in the brain. A common chromosomal disorder that causes androgen deficiency is Klinefelter's syndrome.

AT A GLANCE

How is androgen deficiency diagnosed?

A diagnosis of androgen deficiency involves having a thorough medical evaluation and at least two blood samples (taken in the morning on different days) to measure hormone levels. Diagnosis should not be simply based on symptoms as these could be caused by other health problems that need different treatment.

In a man with clinical features of androgen deficiency, the diagnosis is only confirmed when blood tests show a lower than normal testosterone level and other blood tests show whether it is due to problems in the testes or the pituitary gland.

How is androgen deficiency treated?

Androgen deficiency is treated with testosterone therapy; this means giving testosterone in doses that return the testosterone levels in the blood to normal. Testosterone is prescribed for men with androgen deficiency confirmed by blood tests. Once started, testosterone therapy is usually continued for life and the man needs to be checked regularly by a doctor.

Can I do anything to prevent androgen deficiency?

There are no known ways to prevent androgen deficiency caused by damage to the testes or pituitary gland. However, if your low testosterone levels are caused by other illnesses, adopting a healthier lifestyle and managing other health problems may improve your testosterone levels. Not all men have a drop in testosterone levels with age. A healthy lifestyle may help you to keep testosterone levels normal.



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MALE HORMONES

Androgens are male sex hormones that increase at puberty and are needed for a boy to develop into a sexually mature adult who can reproduce

What are hormones?

Hormones are chemical messengers made by glands in the body that are carried in the blood to act on other organs in the body. Hormones are needed for growth, reproduction and well-being.

What are androgens?

Androgens are male sex hormones that increase at puberty and are needed for a boy to develop into a sexually mature adult who can reproduce. The most important androgen is testosterone.

What is testosterone?

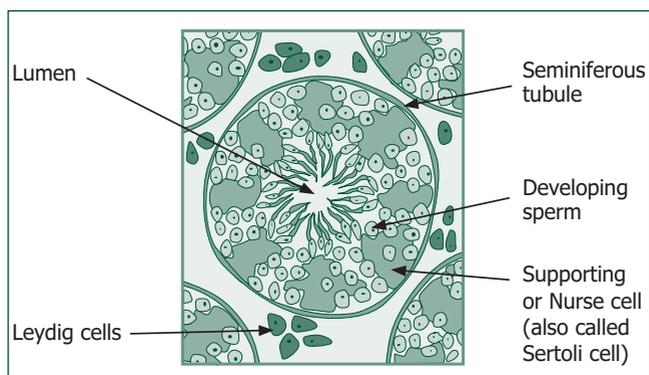
Testosterone is the most important androgen (male sex hormone) in men and it is needed for normal reproductive and sexual function. Testosterone is important for the physical changes that happen during male puberty, such as development of the penis and testes, and for the features typical of adult men such as facial and body hair. Testosterone also acts on cells in the testes to make sperm.

Testosterone is also important for overall good health. It helps the growth of bones and muscles, and affects mood and libido (sex drive). Some testosterone is changed into oestradiol, the female sex hormone, and this is important for bone health in men.

Androgens are male sex hormones that increase at puberty and are needed for a boy to develop into a sexually mature adult who can reproduce.

Where is testosterone made?

Testosterone is mainly made in the testes by cells (the Leydig cells) that lie between the small tubes that make sperm (the seminiferous tubules). Testosterone is carried in the blood to a number of target organs in the body including the skin, hair and muscle. A small amount of testosterone is also made by the adrenal glands, which are walnut-sized glands that sit on top of the kidneys.



Cross-section of a testis showing sperm-producing tubes (seminiferous tubules) and Leydig cells

MALE HORMONES

How do hormones control the testes?

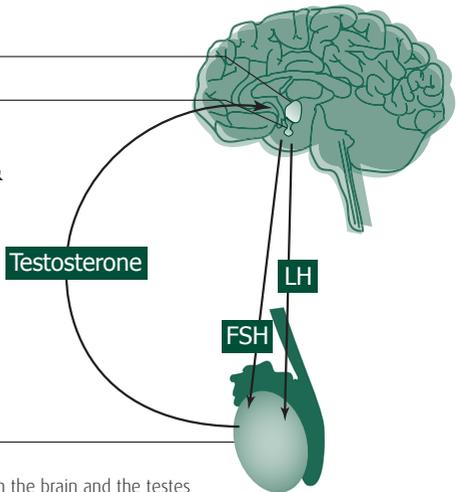
The pituitary gland and the hypothalamus, located at the base of the brain, control the production of male hormones and sperm. The hypothalamus makes gonadotropin-releasing hormone (GnRH), which controls the release of other (messenger) hormones from the pituitary gland. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) are the two important messenger hormones made by the pituitary gland that travel through the blood to act on the testes to make testosterone and sperm.

Hypothalamus

Pituitary

Two hormones from the pituitary - Luteinising (LH) & Follicle Stimulating (FSH) - act on the testis to stimulate production of testosterone and sperm.

Testis



Hormone links between the brain and the testes

What happens to testosterone in the blood?

As testosterone moves through the body in the blood, it is changed or 'metabolised' into other sex hormones, 'oestradiol' and 'dihydrotestosterone' (DHT). Oestradiol, known as the female sex hormone, is also important for male bone health and preventing osteoporosis (thinning of the bones). DHT is a powerful androgen that is made from testosterone in some parts of the body, such as the skin and the prostate.

How do testosterone levels change over the day?

Blood levels of testosterone change across the day. The highest testosterone levels are early in the morning and the lowest levels are late in the evening. This pattern across the day is called a 'circadian rhythm' and happens normally in many of the body's hormonal systems. There is no cycle for men like the monthly female cycle.

MALE HORMONES

How does ageing affect testosterone levels?

Testosterone levels in men are highest between the ages of 20 and 30 years. As men age there is a small, gradual drop in testosterone levels; they may drop by up to one third between 30 and 80 years of age.

This fall in testosterone is now believed to be largely due to the effects of other conditions that men may develop as they age, such as obesity, diabetes and other chronic health disorders. On the other hand, healthy older men with normal body weight do not experience a significant drop in serum testosterone levels.

There is no such thing as ‘male menopause’ or ‘andropause’ that can be compared to menopause in women. Such terms have no medical meaning and are often used by those wishing to promote the use of testosterone in settings where there is no real evidence that it will help, and where the risks are unknown.



ANDROGEN DEFICIENCY

What is androgen (or testosterone) deficiency?

Androgen, or testosterone, deficiency is when the body is not able to make enough testosterone for the body to function normally. Although not a life-threatening problem, androgen deficiency can affect your quality of life.

Testosterone is the most important androgen (male sex hormone) in men.

How common is androgen deficiency?

Androgen deficiency caused by problems in the testes or hypothalamus-pituitary affects about one in 200 men under 60 years of age. It is likely that androgen deficiency is under-diagnosed and that many men are missing out on the benefits of treatment. About one in 10 older men may have testosterone levels lower than those in young men, but this is usually linked with chronic illness and obesity. The risks and benefits of testosterone treatment for such men are not yet known.



Testosterone is the most important androgen (male sex hormone) in men

SYMPTOMS

Symptoms of androgen deficiency include low energy levels, mood swings, irritability, poor concentration, reduced muscle strength and low libido (sex drive)

What are the symptoms of androgen deficiency?

Symptoms of androgen deficiency include low energy levels, mood swings, irritability, poor concentration, reduced muscle strength and low libido (sex drive). Androgen deficiency has different symptoms depending on the age of the man (Table).

Any of these symptoms on their own may not mean you have androgen deficiency. Many illnesses can cause a drop in testosterone levels and some of the symptoms of these illnesses are like the symptoms of androgen deficiency. Low energy levels, low sex drive and mood problems often happen with heart disease, lung problems (including sleep apnoea), diabetes, depression, and brain (dementia) problems.

Stage of Life	Possible symptoms
Early childhood	<ul style="list-style-type: none"> • Penis and testes do not grow to expected size
Early teenage years (puberty)	<ul style="list-style-type: none"> • Failure to go through full normal puberty • Poor development of facial, body or pubic hair • Poor muscle development • Voice does not deepen • Poor growth (height) surge • Breast development (gynaecomastia)
Adulthood	<ul style="list-style-type: none"> • Mood changes (low mood and irritability) • Poor concentration • Low energy • Reduced muscle strength • Increased body fat • Longer time to recover from exercise • Decreased libido (low interest in sex) • Difficulty getting and keeping erections • Low semen volume • Reduced beard or body hair growth • Breast development (gynaecomastia) • Hot flushes, sweats • Osteoporosis (thinning of bones)
Later life (after 60 years)	<ul style="list-style-type: none"> • Mood changes (low mood and irritability) • Poor concentration • Easily fatigued • Poor muscle strength • Increased body fat • Decreased libido (low interest in sex) • Difficulty getting and keeping erections • Breast development (gynaecomastia) • Osteoporosis (thinning of bones)

Symptoms of androgen deficiency at different stages of life

SYMPTOMS

 See Andrology Australia's guide on Erectile Dysfunction for more information

Can androgen deficiency cause erectile dysfunction?

Androgen deficiency can lead to problems with getting and keeping an erection, but it is not a common cause of erectile dysfunction. Erectile dysfunction is more commonly caused by changes to the blood or nerve supply to the penis, for example, in men with diabetes mellitus.

Erectile dysfunction may be an early sign of cardiovascular disease. Performance anxiety, stress and depression may also lead to erectile dysfunction.

Testosterone therapy should not be the first treatment option for erectile dysfunction unless androgen deficiency is diagnosed by a doctor.

When should I see a doctor for androgen deficiency?

See a doctor if you have any of the symptoms listed in the Table. These symptoms may be caused by androgen deficiency or other serious medical problems that need different treatment.

CAUSES

What causes androgen deficiency?

Androgen deficiency can be caused by genetic disorders, medical problems, or damage to the testes or pituitary gland. Androgen deficiency happens when there are problems within the testes or with hormone production in the brain. A common chromosomal disorder that causes androgen deficiency is Klinefelter's syndrome. These problems may happen at any age, or might only be recognised after many years because the symptoms are often subtle or non-specific and androgen deficiency goes undetected.

A common chromosomal disorder that causes androgen deficiency is Klinefelter's syndrome

What are chromosomes?

Chromosomes are found in each cell in the human body. They carry the genetic material (genes) that determines all human characteristics, including hair colour, eye colour, height and sex. Each cell in the human body normally has 23 pairs of chromosomes (a total of 46).

Of the 23 pairs of chromosomes, one pair is called the sex chromosomes because they determine a person's sex. The sex chromosomes in a female are called XX and in a male are called XY. One sex chromosome is inherited from the mother and one from the father. Mothers always pass on an X chromosome, but fathers can pass on an X or a Y chromosome to their children.

CAUSES

What are the genetic causes of androgen deficiency?

Genetic disorders with certain changes to the chromosomes and/or genes can cause androgen deficiency. A common chromosomal disorder that causes androgen deficiency is Klinefelter's syndrome.

What is Klinefelter's syndrome?

Klinefelter's syndrome is a genetic (chromosomal) condition that only affects males. It is congenital, which means it is present from birth. Men with Klinefelter's syndrome have an extra X chromosome. The normal male chromosome arrangement is 46,XY but for men with Klinefelter's syndrome it is 47,XXY.

What are the main effects of Klinefelter's syndrome?

Klinefelter's syndrome is the most common cause of hypogonadism, a condition where men are unable to produce sperm or enough of the male hormone, testosterone, for the body's needs.

The low levels of testosterone in men with Klinefelter's syndrome affect the development of male characteristics. The extra X chromosome also affects the man's ability to produce sperm. Men with this condition are infertile as they almost always have no sperm in their ejaculate (azoospermia).

What problems of the hypothalamus cause androgen deficiency?

A rare genetic disorder known as Kallmann's Syndrome stops the production of gonadotropin-releasing hormone (GnRH), from the hypothalamus (the area in the brain above the pituitary gland). GnRH controls the release of LH and FSH from the pituitary gland. Low levels of LH and FSH from the pituitary lead to less testosterone being made in the testes. Men with Kallmann's Syndrome sometimes have a poor sense of smell.

Rare tumours or other congenital (present from birth) problems of the hypothalamus can also lead to low levels of LH and FSH from the pituitary.

CAUSES

What problems of the pituitary gland cause androgen deficiency?

In rare cases, diseases of the pituitary gland cause low testosterone levels. The most common pituitary disease is a benign (non-cancerous) tumour within the pituitary gland called adenoma. Sometimes adenomas are large enough to put pressure on the normal pituitary cells, stopping them from making the messenger hormones LH and FSH that control the testes.

Sometimes a tumour in the pituitary gland may make too much of another hormone called prolactin, which stops LH and FSH from being released, leading to androgen deficiency. Treatment that lowers prolactin levels may return LH and FSH levels to normal; testosterone would then go back to the normal level.

Surgery or radiotherapy to treat tumours of the pituitary gland may lower LH and FSH levels even more, so that men with a pituitary tumour will often need life-long testosterone therapy.

Can medical problems lower testosterone levels?

Having a major illness will cause a drop in testosterone levels, particularly in ageing men. However, levels usually return to normal when the illness has been treated.

Obesity is strongly linked with lower testosterone levels; on average, very obese men have testosterone levels 25% lower than non-obese men. Weight loss in obese men usually leads to an increase in testosterone levels.

Men with Type 2 diabetes are more likely to have low testosterone levels. However, the role of testosterone therapy when levels are in the low to normal range is not known and researchers are trying to answer this question.

Men with low testosterone levels caused by illness, obesity, diabetes or depression should have treatment for the primary illness first. Once the illness is treated, testosterone levels usually return to normal and testosterone therapy may not be needed.

Weight loss in obese men usually leads to an increase in testosterone levels

CAUSES

What medical problems cause androgen deficiency?

A number of medical problems can cause androgen deficiency either at the time they are diagnosed or later in life. These include:

- Undescended testes, where the testes do not move down into the scrotum before birth. Although this is generally fixed by surgery in the first years of life, medical research has shown that men who had this problem as children have a greater chance of getting testicular cancer, infertility and androgen deficiency after puberty.
- Infections, such as mumps after puberty, can destroy the sperm-producing tubes in the testes and can cause androgen deficiency.
- Cancer treatment, particularly chemotherapy or radiotherapy following testicular cancer, can also damage the sperm-producing tubes in the testes and can cause androgen deficiency.
- Testicular cancer treatment may include the removal of both testes, causing androgen deficiency.

Can depression cause androgen deficiency?

Clinical depression can lead to lower testosterone levels; however, depression should be treated first. Whilst testosterone therapy in men with proven androgen deficiency may improve mood, there is no evidence that testosterone would be useful for treating depression.

Can medicines cause androgen deficiency?

Long-term opiate therapy as treatment for chronic pain or as part of a methadone program will stop the hypothalamus making the hormone GnRH, which in turn can lead to very low testosterone levels.

Can vasectomy cause androgen deficiency?

Vasectomy does not lower testosterone levels in the blood.



STAYING HEALTHY

A healthy lifestyle may help you to keep testosterone levels normal

Can I do anything to prevent androgen deficiency?

There are no known ways to prevent androgen deficiency caused by damage to the testes or pituitary gland. However, if your low testosterone levels are caused by other illnesses, adopting a healthier lifestyle and managing other health problems may improve your testosterone levels. Having treatment for these other medical problems may mean that testosterone therapy is not needed.

Obesity is strongly linked with lower testosterone levels. Weight loss and a healthy lifestyle may help to increase testosterone levels in obese men.

The effect of cigarette smoking on hormone levels is not clear. However, because of this uncertainty, and for other health benefits, a doctor may talk to you about quitting smoking.

Not all men have a drop in testosterone levels with age. A healthy lifestyle may help you to keep testosterone levels normal.



DIAGNOSIS

How is androgen deficiency diagnosed?

A diagnosis of androgen deficiency involves a number of steps:

- a full medical history and physical examination to find a possible cause
- at least two blood samples, taken in the morning on different days, to measure hormone levels
- other tests for certain medical problems known to affect the testes or pituitary gland.

In men with symptoms of androgen deficiency, hormone levels must be tested in a laboratory to confirm that androgen deficiency is the cause of their symptoms.

Diagnosis should not be simply based on symptoms as these could be caused by other health problems that need different treatment.

In a man with clinical features of androgen deficiency, the diagnosis is only confirmed when blood tests show a lower than normal testosterone level and other blood tests show whether it is due to problems in the testes or the pituitary gland.

DIAGNOSIS

What happens when a medical history is taken?

Important clinical features that will be checked by the doctor include:

- general health and well-being (including obesity and diabetes mellitus)
- reproductive history (including development during puberty)
- fertility status
- changes in sexual function, and body and facial hair growth
- use of prescribed medicines, supplements and recreational drugs.

What happens in a physical examination?

A doctor will check secondary sexual characteristics (or the degree of ‘masculinity’) including:

- body hair distribution
- muscle development
- the amount and location of body fat (especially around the abdomen)
- breast enlargement (gynaecomastia)
- measurement of testis size (testes are often smaller with androgen deficiency)
- prostate examination may be done in older men.

What hormones are tested?

A diagnosis of possible androgen deficiency is confirmed by measuring the amount of testosterone in the blood.

Hormones made by the pituitary gland in the brain that act on the testes to make testosterone – luteinizing hormone (LH) and follicle stimulating hormone (FSH) – are also measured.

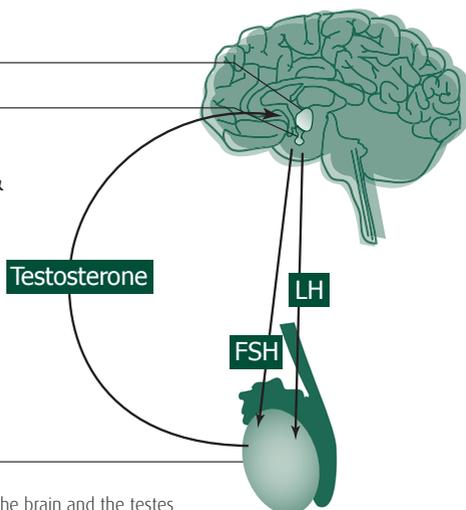
Hypothalamus

Pituitary

Two hormones from the pituitary - Luteinising (LH) & Follicle Stimulating (FSH) - act on the testis to stimulate production of testosterone and sperm.

Testis

Hormone links between the brain and the testes



DIAGNOSIS

A diagnosis of possible androgen deficiency is confirmed by measuring the amount of testosterone in the blood

Testing LH and FSH levels can help with finding the cause of androgen deficiency. If testosterone levels drop, the hypothalamus and pituitary gland respond by making more LH and FSH to activate the Leydig cells within the testes to make more testosterone.

- A low testosterone level together with a higher than normal LH level means that a problem in the testes may be the cause of androgen deficiency.
- Low levels of both testosterone and LH points to a possible pituitary/hypothalamus problem as the cause of androgen deficiency.
- High levels of FSH usually means a sperm production problem. If testosterone levels are also low, a problem with the testes may be the cause of androgen deficiency.

Your doctor may use other measures of testosterone such as the calculated free testosterone.

The FAI (or the free androgen (testosterone) index) should not be used as it is not an accurate measure of androgen levels in men.

Are blood tests needed?

Because hormones are carried in the blood to the target organs, they are measured by taking a blood sample for laboratory testing. A fasting blood sample for measuring testosterone should be taken between 8am and 10am when testosterone levels are at their highest. Testosterone is measured in units called nanomolar. The average testosterone level is 15-20 nanomolar in the morning and about 10-14 nanomolar in the evening.

What is the 'normal' testosterone reference range?

A reference range is used as a guide by testing laboratories and doctors to decide whether a person's hormone levels are normal or low, and whether treatment is needed. The 'normal' testosterone reference range for healthy, young adult men is about 8 to 27 nanomolar but these numbers vary between measurement systems.

Most healthy people (95%) have hormone levels that fall within a standard reference range for their sex. However, a few healthy people (5%) have levels outside the range. Due to this wide variability it needs to be understood that for some normal men, a morning level of 8nM is their ideal level and does not indicate androgen deficiency.

DIAGNOSIS

This is why the diagnosis of androgen deficiency is not based on a simple blood test, but includes a number of steps including a full medical history, physical examination and other tests.

The Endocrine Society of Australia has published guidelines for when testosterone therapy should be used. The Australian Pharmaceutical Benefits Scheme (PBS) uses these guidelines to decide when to subsidise the cost of testosterone therapy.

What other tests for androgen deficiency might be done?

Sometimes tests to check for medical problems that affect the function of the testes are needed. Information from these tests may affect the way that androgen deficiency is treated.

- Karyotype: to look at the number and structure of the chromosomes to check for Klinefelter's syndrome or other chromosome or genetic problems.

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- Semen analysis: to check fertility.
 - MRI or CT scan: to look at the pituitary gland in the brain to see if it is the cause of the problem.
 - Prolactin testing: to measure the amount of the hormone prolactin (made in the pituitary gland) in the blood. Higher levels of prolactin could be a sign of a benign (non-cancerous) tumour (adenoma) in the pituitary gland. High prolactin levels stop the LH and FSH from being released.
 - Iron studies: to measure possible iron overload in the testes or pituitary that is caused by too much iron being stored (haemochromatosis), or multiple blood transfusions for chronic anaemia (such as thalassemia).
 - Sleep studies: to test breathing patterns if sleep apnoea (short periods when breathing stops during sleep) may be present.

DIAGNOSIS

Why is bone density testing done when androgen deficiency is diagnosed?

Testosterone is important for developing and maintaining bone strength. After puberty, men with androgen deficiency have a higher risk of osteoporosis (thinning of the bones), which leads to a greater chance of fracturing bones, especially in the hip and the spine. Osteoporosis does not usually have external symptoms, so a bone density test (DEXA scan) may be needed to check the bones.

Calcium and Vitamin D are both important for bone health. You may need to take dietary supplements if your calcium and/or Vitamin D levels are low.

Will I need to see a specialist for androgen deficiency?

General practitioners (GPs) can make a diagnosis of androgen deficiency. There are new regulations for doctors when prescribing testosterone treatment that is supported by the Pharmaceutical Benefits Scheme (PBS, April 2015). Because of these new regulations, your GP will refer you to see an endocrinologist or other appropriate specialist. After this, your GP can monitor your treatment and prescribe testosterone therapy in conjunction with the specialist.



TREATMENT

Androgen deficiency is treated with testosterone therapy

How is androgen deficiency treated?

Androgen deficiency is treated with testosterone therapy; this means giving testosterone in doses that return the testosterone levels in the blood to normal. Testosterone is prescribed for men with androgen deficiency confirmed by blood tests. Once started, testosterone therapy is usually continued for life and the man needs to be checked regularly by a doctor.

When should I talk to my doctor about testosterone therapy?

Testosterone therapy helps men of any age with known causes of androgen deficiency.

Your doctor may also talk to you about weight loss, lifestyle changes, treatment of other serious illness (such as diabetes), and medicines you are taking. You should also talk to your doctor about work or relationship issues that may be affecting your health.

Should I seek a second opinion before starting treatment?

A second opinion is always helpful if you feel uncomfortable about any suggested treatments or if the way you are treated seems unusual.

Here are some situations where a second opinion might be helpful.

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- The direct sale of testosterone from the doctor: testosterone treatments are not expensive and are available on the PBS as long as you meet the guidelines.
 - Suggestion by the doctor to use locally compounded testosterone preparations: you should ask the doctor about how well these compounded testosterone preparations work compared to commercial testosterone preparations approved by the Australian Therapeutic Goods Administration (TGA) after careful clinical testing.
 - Suggested treatment with doses higher than those recommended in this booklet: such doses are called ‘supraphysiological’. While they may help your symptoms, they may not be safe.
 - You feel that you are under pressure to make long-term financial commitments.
 - You feel you are not being offered proper ongoing review and care of problems.
 - Treatment is suggested following a single appointment or blood test: correct diagnosis needs blood testing on at least two separate visits.
 - You feel that the consultation is only focused on testosterone levels and does not cover general health, lifestyle and other possible illnesses.

Men can benefit from testosterone therapy when androgen deficiency has been diagnosed and confirmed with blood tests.

TREATMENT

What happens if androgen deficiency is not treated?

Androgen deficiency is generally not a life-threatening medical problem. Many men with androgen deficiency are undiagnosed and live without treatment; however, they may have a lower quality of life and might get other health problems such as osteoporosis (thinning of the bones).

Who should have testosterone therapy?

Any man who has a confirmed diagnosis of androgen deficiency should be treated as long as there are no other health problems, such as prostate cancer, that make it risky to give treatment.

Testosterone therapy has been shown to have positive effects on body fat, muscle, cholesterol, bone density and quality of life.

Although not strictly within the range for a diagnosis of androgen deficiency, some men with testosterone levels between 8 and 15 nanomolar may also benefit from testosterone therapy.

The Endocrine Society of Australia guidelines are used by doctors when deciding to prescribe testosterone therapy, while the PBS has rules for eligibility for subsidised testosterone therapy. If your doctor prescribes testosterone outside the PBS criteria, it is legal and not very expensive.

Should older men have testosterone therapy?

As in younger men, older men may have testicular or pituitary disease that leads to low total testosterone levels. Testosterone treatment for these men will help to lower body fat and cholesterol, improve muscle tone and bone density, and improve quality of life and sexual function.

The major controversy for testosterone treatment in older men is understanding the risks and benefits when the low testosterone levels are due to other conditions such as diabetes or obesity. Ongoing research is looking at whether there is a safe and effective role for testosterone in older men.

Who should NOT have testosterone therapy?

An important concern when prescribing testosterone therapy is prostate disease. Testosterone therapy may cause the prostate gland to grow. Men with prostate enlargement (benign prostatic hyperplasia, BPH) and severe lower urinary tract obstruction need to be checked by a doctor before starting treatment.

TREATMENT

Testosterone therapy is not known to cause new prostate cancer but may make unrecognised prostate cancer grow

Testosterone therapy is not known to cause new prostate cancer but may make unrecognised prostate cancer grow. Older men should be checked for prostate cancer before starting treatment. Men with advanced prostate cancer who have had medical or surgical castration (removal of the testes to lower the amount of testosterone in the body) should not be treated with testosterone. Testosterone therapy should not be prescribed for men with breast cancer.

Testosterone therapy should not be the first treatment if low testosterone levels are caused by other medical problems such as obesity, diabetes mellitus or depression. These underlying problems should be treated first, as hormone levels may return to normal and testosterone therapy may never be needed.

Testosterone therapy will stop any sperm production because it turns off the hormones (FSH and LH) from the brain that drive sperm production. Therefore testosterone treatment should not be given to a man wanting to father a child; they should be referred to a specialist to talk about ways to keep their fertility (such as sperm freezing) prior to beginning lifelong treatment for their androgen deficiency.

Testosterone should not be used in young boys (who have not completed natural puberty) without talking to a paediatric endocrinologist.

Testosterone therapy should not be endorsed, requested or prescribed as a 'cure-all' for symptoms of ageing.

What are the main forms of testosterone therapy?

In Australia testosterone therapy is available in the form of injections, gels, lotions, creams, patches and tablets, and it works very well for men with confirmed androgen (testosterone) deficiency. The type of treatment prescribed can depend on patient convenience, familiarity and cost.

Commercial testosterone products contain only the natural testosterone molecule that is chemically produced from plant materials.

Testosterone injections (Primoteston®)

Testosterone injections (250 mg in 1 mL) are given into the muscle, usually the buttock, every two to three weeks, depending on the dose needed and the man's response. Injections of 250 mg are standard treatment, although lower doses may be used.

TREATMENT

Some men who are sensitive to the peaks (high levels of testosterone) and troughs (low levels of testosterone) across the weeks, or find the injections painful, should talk to the doctor about other ways of giving testosterone.

Testosterone injections should not be given to men with bleeding disorders or those taking anticoagulants (blood thinning medicines).

Long acting testosterone injections (Reandron® 1000)

Long acting testosterone injections (1000 mg in 4 mL) are given into the muscle in the buttock and last between 10 and 14 weeks. After the first injection, a second injection is given at 6 weeks and from then on, about every 12 weeks; the dose interval is reviewed regularly by the doctor. The testosterone is released slowly so that men are less likely to have the peaks and troughs common with standard injections.

Long acting testosterone injections should not be given to men with bleeding disorders or those taking anticoagulants (blood thinning medicines).

Testosterone gel (Testogel®)

Testosterone gel is rubbed into the skin once a day. When the gel is applied to the shoulders, arms or abdomen, testosterone is absorbed into the skin,

which acts as a reservoir. The testosterone moves into the blood slowly to keep an even dose over 24 hours.

Try to avoid close physical contact for six hours after applying the gel because there is a chance it will transfer to another person. Wash hands with soap and water after applying the gel and cover the area with clothing. For best absorption of testosterone, it is best not to shower or run for six hours after you apply the gel.

However, if you are likely to come into close physical (skin to skin) contact with someone in that time it is best to have a shower beforehand.

Avoiding person to person transfer of testosterone is especially important for children and pregnant women.

Testosterone lotion (Axiron®)

Testosterone lotion is applied to the skin of the axilla (armpit). Testosterone lotion provides blood testosterone levels that are like that from gels. Try to avoid another person having close physical contact with the area where you have applied testosterone lotion because there is a chance it will transfer to the other person. Wash hands with soap and water after applying the lotion and cover the area with clothing. Testosterone lotion (Axiron®) has been approved for use by the Australian TGA and is listed on the PBS.

TREATMENT

Testosterone patches (Androderm®)

Testosterone is available in patches that are put on at night and worn at all times to allow testosterone to be absorbed through the skin. The normal dose is a single 5 mg patch but 2.5 mg patches are also available to allow some adjustment to the dose. The patches are put on to the back, arm, shoulder, abdomen or buttocks.

About one in ten young men and about one in five older men develop a skin rash when using the patches. If you have a problem with skin rashes, changing the place where you put the patch and/or using cortisone cream (Aristocort® cream, 0.02% triamcinolone) under the patch may help.

Testosterone cream (AndroForte®)

There are two versions of testosterone cream: AndroForte® 2 contains 20 mg of testosterone in 1 mL of cream. This is applied directly to the scrotum. AndroForte® 5 contains 50 mg testosterone in 1 mL of cream and is applied to the torso. The cream is absorbed through the skin or the scrotum into the body. Your doctor will talk to you about which cream would be better for you. As for gels and lotions, testosterone cream can transfer to other people through physical contact and this should be avoided.

Oral testosterone undecanoate (Andriol®)

These 40 mg capsules must be taken with fluid or food that contains fat (such as milk) to help you absorb the testosterone. One or two tablets are taken three times each day. The testosterone levels from this form of treatment often do not fully replace the testosterone. Oral testosterone is only chosen when other forms of testosterone are not suitable. The capsules may be a good way to start treatment slowly if your testosterone levels have been low for a long time.

Other testosterone preparations

Some oral preparations (medical lozenges or troches), may be produced by compounding chemists. However, these are not government approved and it is not clear how well they work. An oral preparation, which is placed inside the mouth (buccal) and absorbed through the membranes lining the gums, is available overseas and not yet available in Australia.

TREATMENT

 See Andrology
Australia's guide on
Prostate Enlargement
for more information

What are the side-effects of testosterone therapy?

Side-effects are not expected because testosterone therapy aims to bring a man's testosterone levels back to normal. However, testosterone therapy can increase the growth of the prostate gland which can make the symptoms of benign prostate enlargement worse (for example, needing to urinate more often). In the case of prostate cancer, testosterone therapy is not used because of concerns that it can make the tumour grow.

Too high a dose of testosterone can lead to acne, weight gain, gynaecomastia (breast development), male-pattern hair loss and changes in mood. Any side-effects should be managed by a doctor and the testosterone dose lowered.

Sometimes testosterone therapy can increase the number of red blood cells (polycythaemia) leading to problems with blood circulation. This is more likely to be a problem for older men, especially if they have sleep apnoea (short periods where breathing stops during sleep that is often found in men with heavy snoring), or for men who smoke.

Sleep apnoea, migraine symptoms (in men who get migraines) or androgen-sensitive epilepsy can also get worse with testosterone therapy. The major concern with testosterone therapy in ageing men is that testosterone can make unrecognised prostate cancer grow.

When should testosterone therapy be stopped?

If androgen deficiency is diagnosed at any age, testosterone therapy will usually be needed for the rest of the man's life. However, at this stage, there is no evidence for benefit from testosterone therapy if a diagnosis of androgen deficiency has NOT been confirmed by laboratory tests.

If a man who does not have androgen deficiency starts testosterone therapy, his body will stop making its own testosterone. If he later stops treatment, he may have symptoms of low testosterone for a period of time as his testes gradually begin to make testosterone again.

The withdrawal and review of testosterone therapy should be done under medical supervision.

Too high a dose of testosterone can lead to acne, weight gain, gynaecomastia (breast development), male-pattern hair loss and changes in mood

TREATMENT

Where can I get testosterone from?

When you are diagnosed with confirmed androgen deficiency a doctor can prescribe testosterone in any of the available forms, which can be obtained from a pharmacy.

It is possible for doctors or pharmacists to apply to the Australian Therapeutic Goods Administration (TGA) for a permit to import testosterone from overseas. Testosterone is currently on the banned import list and the Australian Customs Service can give information on how it can be imported legally.

Where else can men purchase testosterone from?

Claims are made for many natural products to help low testosterone levels. Some doctors use locally compounded testosterone preparations. You should ask the doctor about how well these compounded testosterone preparations work compared to commercial testosterone that is approved by the TGA (only after careful clinical testing).

Men must be aware that if buying tablet medicines on the Internet, they could be buying useless and dangerous versions of the medicines. There are global spam merchants, who sell counterfeit drugs on the Internet at discounted prices, but there is no guarantee that they work and their safety is not known.

Are there other androgen supplements?

Fluoxymesterone and 17-alpha-methyl testosterone are synthetic androgens. These may cause liver damage and are not suitable for treating androgen deficiency and should not be used. These androgens are not available through the PBS in Australia.

What other supplements may be offered to men with symptoms of androgen deficiency?

Growth hormone supplements have been promoted as 'anti-ageing' products but no real benefit has been shown. The risks of taking growth hormone on a long-term basis are also not known. Growth hormone is therefore not recommended as a treatment for androgen deficiency.

DHEA (dehydroepiandrosterone) and androstenedione are very weak androgens made by the body. These hormones do not work well when used to treat androgen deficiency and they are not approved for this purpose in Australia.

TREATMENT

Can herbal products help androgen deficiency?

There are many herbal products marketed, particularly on the Internet, as treatments that can act like testosterone and improve muscle strength and libido (sex drive). However, there are no known herbal products that can replace testosterone in the body and be used to treat androgen deficiency.

What regular checks are needed when having testosterone therapy?

All men who have testosterone therapy need to have regular visits with their doctor to check how well the treatment is working and to make sure there are no side-effects. This examination often includes blood tests. In particular the amount of haemoglobin (red blood cells) may increase, leading to a higher risk of blood clots. If this happens, the dose will need to be lowered.

Older men need to be checked for prostate cancer before testosterone therapy is started because testosterone can make unrecognised prostate cancer grow.

For men with thinning bones, regular checks of bone density (DEXA scan) will be needed.

Will testosterone therapy affect my fertility?

Testosterone therapy generally stops the production of the pituitary hormones FSH and LH, which reduces the size of the testes and can lower or stop sperm being made. Testosterone treatment should not be given to a man wanting to become a father in the foreseeable future. If sperm production was normal before testosterone therapy, it usually recovers after treatment stops but it can take many months to go back to normal.

Men who have androgen deficiency caused by a medical problem that affects the testes don't usually make sperm and may already be infertile before treatment starts.

Testosterone therapy does NOT boost sperm counts and men with fertility issues should talk to their doctor before starting treatment. Men with low sperm counts wishing to have children may be helped by other hormonal treatments (that act like LH and FSH) that increase sperm and testosterone production.

 See Andrology Australia's guide on Male Infertility for more information

TREATMENT

When is other hormone therapy needed?

A man who wants to have a child but has low levels of pituitary hormones (and no underlying damage to the testes), can have injections to replace the pituitary hormones LH and FSH which will increase his sperm count. This treatment will also bring testosterone levels back to normal. After fertility treatment is complete, these men are then prescribed standard testosterone therapy alone.

Men with damage to the pituitary gland may also need other hormone treatments such as thyroid hormone or cortisol.

Will testosterone therapy affect the size of the testes or penis?

If testosterone is taken before puberty (under the care of a paediatrician) to treat micropenis (very small penis size), the penis will grow to a normal adult size. If testosterone is given during normal puberty or adulthood, there will be no further change in penis size. However, the testes may get smaller because the testosterone turns off the pituitary hormones.

Will testosterone therapy affect sporting performance?

Testosterone therapy in men with androgen deficiency aims to bring testosterone levels back to normal and to return muscle strength and energy levels back to normal. However, the use of androgens (anabolic steroids) by normal men to improve athletic performance is illegal and has important short-term and long-term health risks.

Men who use anabolic steroids will lower or even turn off their own testosterone and sperm production. It may take many months for testosterone levels and sperm counts to return to normal after stopping anabolic steroids.

The testes may get smaller when using anabolic steroids.

Competitive athletes who take part in drug screening in their sport should be warned about the risks of disqualification if testosterone is prescribed for medical treatment. Special exceptions may be given by the Australian Sports Drug Medical Advisory Committee for elite athletes who need testosterone treatment for genuine medical problems, such as Klinefelter's syndrome.



Men who use anabolic steroids will lower or even turn off their own testosterone and sperm production

SUPPORT

This booklet gives information about androgen deficiency and may be helpful when talking with your doctor. It is not possible to guess if you are suffering from androgen deficiency as symptoms may be due to other medical problems. You will need to talk to your local family doctor about any health concerns.

There are not many support groups or other resources for men suffering from androgen deficiency. For general support, contact your local council or your local doctor to see if there is a community men's health program in your area.

For men with Klinefelter's syndrome, information and support is available in Australia and online from overseas organisations.

Genetic Alliance Australia (formerly AGSA) is a peak umbrella group for rare genetic conditions. It offers a range of support options for people with genetic conditions, including Klinefelter's syndrome.

Tel: **(02) 9295 8359**

Email: **info@geneticalliance.org.au**

Australian X and Y Spectrum Support aims to help individuals and families affected by Klinefelter's syndrome and other sex chromosome variations. They bring together Australian State groups and are supported by AXYS (Association for X & Y Chromosome Variations, USA).

Email: **contact@axys.org.au**

Hormones and Me: Klinefelter syndrome is a booklet produced by Serona Symposia International with the Australasian Paediatric Endocrine Group (APEG). It is available from APEG (www.apeg.org.au) and Andrology Australia (www.andrologyaustralia.org).



Websites



Genetic Alliance Australia

www.geneticalliance.org.au



Australian X and Y Spectrum Support

<http://axys.org.au>



Andrology Australia

www.andrologyaustralia.org



Endocrine Society of Australia

www.endocrinesociety.org.au



Association for X & Y chromosome variations (AXYS) USA

www.genetic.org



Klinefelter's Syndrome Association (KSA) UK

www.ksa-uk.net



Please note that websites developed overseas  may describe treatments that are not available or approved in Australia . If you have any questions about information found on these or other sources please talk to your doctor.

GLOSSARY

adenoma A benign (non-cancerous) tumour having the origin or structure of a gland

androgen A male sex hormone such as testosterone

benign Non-cancerous

cancer Disease in which abnormal cells divide without control. Cancer cells can spread to nearby tissues and through the blood and lymphatic systems to other parts of the body

castration Removal of the testes

chromosomes Structures in each cell in the body that carry genetic information. Humans normally have 46 chromosomes in each cell

circadian rhythm A pattern based on a 24-hour cycle

CT (computerized tomography) scan A specialised X-ray taking many cross-sectional images (combined to make 3-dimensional images) of organs in the body to help find abnormal changes within them

DHEA (dehydroepiandrosterone) A weak androgen

DHT (dihydrotestosterone) A powerful androgen made from testosterone in some parts of the body

endocrine system The body system made up of glands (including the pituitary, thyroid, adrenals, testes) that release hormones (chemical messengers) into the blood to be carried to other organs in the body

endocrinologist A doctor who specialises in problems of the endocrine system (hormones and body functions controlled by hormones). A paediatric endocrinologist cares for children with problems of the endocrine system

fertility Being able to conceive or reproduce

FSH (follicle stimulating hormone) A hormone from the pituitary gland that helps the testes to make sperm

gynaecomastia Breast development in males

hormones Chemical messengers made by glands in the body that are carried in the blood to act on various organs. Hormones are needed for growth, reproduction and well-being

hypogonadism A condition where the testes are not able to make enough testosterone (androgen deficiency) and/or sperm (spermatogenesis)

hypothalamus The area of the brain that controls endocrine functions, body temperature, hunger and thirst

karyotype A blood test to check the number and structure of chromosomes in cells

Klinefelter's syndrome A genetic problem that causes low testosterone levels, breast development, small testes and infertility in men

Leydig cells The cells in the testes that make the male hormone testosterone

GLOSSARY

LH (luteinizing hormone) A messenger hormone made by the pituitary gland that acts on the Leydig cells in the testes to make testosterone

menopause When menses (periods) stop in women

micropenis When penis size is much smaller than normal. Micropenis happens when the penis does not grow for the last two-thirds of development before birth

MRI (magnetic resonance imaging) scan A specialised non-invasive medical imaging process, which does not use X-rays, used to diagnose a wide range of diseases

nanomolar Unit of measurement (used in measuring testosterone)

oestradiol The major female sex hormone made by the ovary but also made in smaller amounts in the testes and has an important role in a man's bone health.

orchidectomy The surgical removal of one or both testes

osteoporosis Thinning of bones that leads to a greater chance of breaking bones

PBS (Pharmaceutical Benefits Scheme) Australian Government program that pays in part the cost of some prescribed medicines to make them cheaper for the consumer

pituitary gland A small gland that sits at the base of the hypothalamus, which is part of the brain

prolactin A hormone made and released into the blood by the pituitary gland

puberty The period in both males and females when changes happen in reproductive organs (ovaries and testes) so that reproduction is possible

seminiferous tubules The small tubes in the testes that make sperm

sleep apnoea (apnea) A condition where breathing stops for a short time during sleep

sperm Male sex cell

testis/testicle (plural: testes) The male reproductive organ that makes sperm and male sex hormones

testosterone Male sex hormone (androgen)

TGA (Therapeutic Goods Administration) Australia's regulatory authority for therapeutic goods (including prescribed medicines and other medical treatments)

undescended testis A condition where the testis does not move down (descend) from the groin or abdomen into the scrotum before birth. Also known as cryptorchidism

vasectomy A medical operation in which the vas deferens (the tube that carries sperm) is cut to make a man sterile



EXPERT REVIEWERS

Andrology Australia gratefully acknowledges the expert panel and consumers with androgen deficiency who gave helpful input into the original production of this guide.

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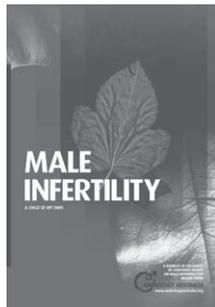
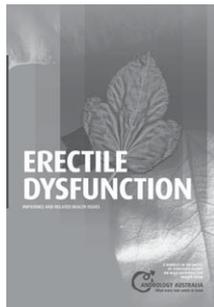


Andrology Australia (The Australian Centre of Excellence in Male Reproductive Health) gives free independent and evidence-based information and education to the community and health professionals on disorders of the male reproductive system and associated problems.

Andrology Australia's resources and information are provided at no cost and are available to be downloaded or ordered online at **www.andrologyaustralia.org** or ordered by phone **1300 303 878**.



Other booklets available in the Andrology Australia Consumer Guides Series on men's health include:





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Andrology Australia (The Australian Centre of Excellence in Male Reproductive Health) is supported by funding from the Australian Government Department of Health and is administered by Monash University.