Hypogonadism

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What is hypogonadism in men?

Hypogonadism in men describes a condition where there is not enough testosterone (called androgen deficiency) and/or a normal number of sperm.

Testosterone and sperm are made by the testes. Their production is controlled by parts of the brain called the hypothalamus and pituitary gland.

Testosterone is responsible for many male characteristics, such as growth of facial and body hair, muscle mass and sex drive (libido). Men with hypogonadism can experience symptoms and signs from their low testosterone levels and reduced fertility (an inability to naturally father children) because of low sperm production.

Hypogonadism can affect men at any age. The most common cause of hypogonadism in Australia is Klinefelter syndrome, affecting about 1 in 450-700 men.[1] Other causes are less common.

What causes hypogonadism in men?

Primary hypogonadism
Primary hypogonadism results from conditions affecting the testes, resulting in low testosterone and reduced fertility.[2] This includes:

- Undescended testes (where the testes are not felt in the scrotum)
- Absent testes (anorchidism)
- Infections of the testes, for example, mumps
- Testicular injuries
- Tumours of the testes
- Cancer treatment (chemotherapy or radiotherapy to the testes)
- Genetic conditions such as Klinefelter syndrome or Y chromosome microdeletion.

Secondary hypogonadism
Secondary hypogonadism is caused by conditions that affect the hypothalamus and/or the pituitary gland.[2] In these cases, the testes do not receive the signals needed to make testosterone and sperm. This is because the hypothalamus and pituitary gland don't make enough of the hormones called luteinising hormone (LH), or follicle stimulating hormone (FSH).

Examples of conditions related to the hypothalamus and/or pituitary include:

- Tumours (and their treatments) of the pituitary gland.
- Genetic conditions, for example: Kallmann syndrome, Prader-Willi syndrome, hemochromatosis.

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Other causes of low testosterone levels in men

Older age

Healthy older men who do not have disorders of the hypothalamus, pituitary or testes can have lower levels of testosterone in the blood compared with younger men. For most men, this is of no concern unless accompanied by symptoms or signs of testosterone deficiency.

Older men as a group tend to have lower testosterone levels compared with younger men.[3] A common myth is this represents a "male menopause" or "andropause". However, these terms have no medical meaning.

In women, menopause happens quite quickly, with a sudden drop in sex hormone levels signifying the end of her reproductive years (typically around age 50 years). This is very different from the gradual decline in testosterone that occurs in some men over time.[4] The use of these terms in reference to men is misleading, and often used to promote testosterone replacement therapy for reasons other than hypogonadism, where there is no evidence of benefit.

Research suggests that some men might not experience a fall in testosterone as they age.[5] An age-related fall in testosterone may therefore not be due to ageing itself, but rather due to other medical conditions that accumulate with ageing, in particular obesity.[6] In these men, a low testosterone level may be a marker for general poor health.[7] The best way to maintain testosterone levels during the transition from middle to older age may be to engage in healthy lifestyle behaviours and avoid excess weight gain.[8,9,10]

Weight

Men who are overweight at any age can have lower levels of testosterone in the blood, without any disorders of the hypothalamus, pituitary or testes.[6]

Other health conditions and medication

There are several conditions that cause reduced function of the hypothalamus and pituitary gland without affecting their structure. This can include mental health disorders such as depression. Some medications, such as glucocorticoids (commonly called "steroids", for example prednisolone) and opioids (for example, morphine), can also reduce the function of the hypothalamus and pituitary gland, or directly impact the ability of the testes to produce testosterone.

In these circumstances, treatment is best directed at the underlying disorder, adjusting medications or trying non-drug therapies.

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Anabolic-Androgenic steroids
Abuse (or misuse) of these drugs can shrink the size (volume) and impair the function of the testes. This can result in lower testosterone levels and reduced sperm production, which can lead to infertility, mood disturbance and sexual problems. These effects are usually reversible after stopping anabolic steroid use, although the recovery time depends on the length of time and dose they were taken.[11]

What are the symptoms and signs of hypogonadism?

Hypogonadism results in testosterone deficiency and low sperm production. The symptoms and signs of testosterone deficiency depend on the age when it first occurs, its severity and duration.

Symptoms and signs observed in early childhood most often are present (but unnoticeable) before birth.

Early Childhood
- Penis and testes are very small, and do not develop normally.

Puberty
- Delayed puberty
- Little growth of facial, body and pubic hair
- Voice doesn't deepen
- Greater than normal growth of bones of the arms and legs
- Undescended testes
- Very small penis
- Breast development / enlargement

Adulthood
- Reduced bone health (bone thinning and weakness, fractures, loss of height, osteoporosis)
- Breast development / enlargement
- Difficulty getting and maintaining erections
- Soft, small testes
- Low sperm count
- Reduced growth of facial or body hair

Some symptoms have multiple causes but are common in men with low testosterone[10].

These include:
- Decreased libido (sex drive)
- Erectile dysfunction
- Loss of muscle mass and strength
- Increased body fat (particularly around abdomen/stomach)
- Lethargy/fatigue
- Low energy levels
- Longer time to recover from exercise
- Irritable and low mood
- Poor concentration
- Short term memory difficulties
- Hot flushes

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How is androgen deficiency diagnosed?

A series of tests are required to carefully diagnose the cause of hypogonadism[10], [12]. This ensures the best treatment is given for each person based on their needs.

1. Medical History and Physical Examination

Your doctor may ask you questions about:

- your current health and medical history (smoking, drugs, alcohol, medications, including anabolic steroids and natural therapies or supplements)
- your reproductive health (undescended testes, genital abnormalities, puberty timing and development, fertility, erectile function, interest in sex, any previous pelvic surgery, genital trauma or infection)
- any symptoms of testosterone deficiency

The physical examination may include measurements of height, weight, waist circumference, a check for enlarged breasts, assessments of body hair and muscle mass, and examination of the scrotum (to assess the volume of testes). Some doctors might test whether you can see objects at the periphery of your vision (as this might indicate a pituitary problem) or whether you cannot smell properly (as this might indicate Kallmann syndrome).

2. Testosterone measurement

If symptoms and signs suggest hypogonadism, your doctor will do a blood test. This is to measure the level of testosterone in the blood, as well as other hormones that control the production of testosterone. These include luteinising hormone (LH) and follicular stimulating hormone (FSH). In blood, testosterone is attached to a protein called 'sex hormone binding globulin' (SHBG). This can also be measured in the blood sample as it can be helpful when interpreting the testosterone result.

This involves taking a small amount of blood (usually in the morning after an overnight fast) and sending it to pathology for lab tests. These results need to be confirmed in a repeat blood test, as a single measurement is not conclusive.[2]

3. Additional blood and genetic testing

These tests may be conducted to identify the cause of low testosterone.[2] These include:

- Measuring levels of prolactin. This is to check for a pituitary tumour (prolactinoma) which interferes with the pituitary signalling to the testes.
- Iron levels. This is a check for haemochromatosis – a genetic condition resulting in high iron levels, which can affect pituitary function.

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- Karyotyping. This is used to assess the number, size and shape of the chromosomes to check for genetic conditions (such as Klinefelter syndrome).
- Y Chromosome microdeletion test. This is used to check whether parts of the Y chromosome are missing.

4. Semen analysis

If you are planning to father a child, your doctor may recommend you have a semen analysis to assess your fertility. For this test, your doctor will refer you to a clinic or pathology provider conducts semen analysis. The clinic will provide instructions for the semen collection. In most cases, semen collection is conducted in a private room in the clinic, as a fresh sample is needed for testing (collected within one hour). Semen is generally collected into a specimen jar following ejaculation by masturbation, although other methods are available. The results will include sperm concentration (count) sperm shape and sperm motility (or movement). These factors can indicate your chances of having a child naturally.

5. Pituitary function tests and imaging

If pituitary disease is suspected, your doctor may wish to check that other hormones are being produced normally by the pituitary, to maintain normal function of the adrenal and thyroid glands.

This can be achieved by measuring the amount of cortisol in a blood sample taken first thing in the morning, and the amount of thyroid hormone. The best way to image the pituitary is by having a magnetic resonance imaging (MRI) scan of the pituitary. If MRI is not feasible, some information can be obtained by a high-quality CT scan of the pituitary instead.

6. MRI Scan

Your doctor may choose to send you for a MRI (magnetic resonance imaging) to check the size and shape of your pituitary. A MRI scan uses a magnetic field and radio waves to take pictures of parts of the body. In general, before having an MRI, you will change into a cotton gown, and need to remove any watches, jewellery and other metallic objects. You may be given earplugs or headphones, as the machine can be quite noisy. Some people with metal in their body (for example, certain pacemakers, or welding injuries with metallic foreign bodies in their eyes) cannot have an MRI.

For the scan, you will lie on a platform that slides into the MRI machine. This is shaped like a cylinder and made of large magnets. When the machine is turned on, these magnets create the magnetic field. You will need to lie very still while inside the machine, as movement can blur the images.

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When inside the MRI machine, you will still be able to talk to the operator through an intercom system. The scan can take up to an hour.

7. Bone mineral density (BMD) test
Your doctor may test your bone mineral density. This is because androgen deficiency can increase the risk of osteoporosis (thinning and weakening of the bones). The best way to test bone mineral density is using a DEXA scan (Dual Energy X-ray Absorptiometry scan). This is a fairly quick (10-30 minutes) and painless procedure. It involves lying fully clothed on a platform while a scanner passes over you to take pictures of your hip and spine.

How is hypogonadism treated?

Treatment depends on the underlying cause of hypogonadism, as incorrect treatment can have serious side effects.

Fertility
It is important to let your doctor know if you want to father a child in the near future (for example, the next 1-2 years). In this case, treatment for reduced fertility takes priority over starting testosterone treatment. This is because testosterone replacement treatment does not improve fertility. In fact, testosterone replacement treatment may reduce sperm count and reduce the chance to father a child. However, some men may still be fertile while taking testosterone, so contraception/protection is still needed if they do not wish to have a baby.

Treatment to improve fertility depends on the type of hypogonadism (primary or secondary). There are different medications that can be successful for some men but can take many months to work. Your doctor will usually refer you to a fertility specialist to do a full assessment, prescribe treatment and monitor the response.

Testosterone deficiency
For men with testosterone deficiency due to hypothalamic, pituitary or testicular disorders, testosterone replacement therapy is usually needed. The main goal of this treatment is to improve symptoms.
In Australia, there are two main ways to receive testosterone replacement therapy.[12]

- Testosterone gel or cream- applied daily onto the skin.
- Testosterone injections - into the gluteal muscle by a health care professional, usually administered every 3 months.

Care must be taken to cover the skin after using gel or cream and wash your hands thoroughly after the application.

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This is to avoid accidentally transferring the testosterone to other people, particularly those you have close physical contact with, for example, partner or children.

Side effects of treatment include pain or bruising at the injection site (for injections), skin irritation (for gel or cream), an increase in red blood cells (polycythemia), increased prostate specific antigen (PSA) levels, mild acne and oily skin and male pattern balding. Breast enlargement (gynaecomastia) is uncommon but may occur. Giving testosterone treatment reduces sperm count and reduces fertility which is why men with hypogonadism who want to father children should not be started on testosterone until after this is addressed (see 'fertility' above).

Your doctor will usually conduct regular follow-up appointments to make sure your symptoms are improving and monitor your testosterone level by doing blood tests. Every 1-2 years, a bone mineral density scan may be performed to check your bone health. Monitoring a PSA level to check for prostate cancer may also be conducted, depending on your age and whether any other risk factors for prostate cancer are present.

In general, testosterone therapy should not be used in men with prostate cancer or breast cancer, or those planning to father a child in the near future.

Sometimes men can be offered testosterone replacement therapy from friends (for example, at the gym) or purchase it over the internet. These formulations are not approved by the Therapeutic Goods Association and may contain a different dose or even type of medication to what is stated on the label. It is strongly recommended to only take approved formulations of testosterone that are prescribed by a specialist doctor.

FAQs about hypogonadism

Is hypogonadism an inherited condition?
Not in most cases, although there are some rare inherited conditions that can cause hypogonadism, such as haemochromatosis.

How long do I have to take my medication?
In most cases, testosterone replacement therapy for men with testosterone deficiency due to pituitary or testicular disease is a lifelong treatment.

Does testosterone replacement therapy cause prostate cancer?
There is no convincing evidence that shows testosterone replacement therapy causes any type of cancer. Men who are treated

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with testosterone replacement therapy are monitored closely by their doctors. This often includes checks of a PSA level. Increased monitoring means there is an higher chance of over-diagnosing insignificant prostate cancers, or finding a pre-existing cancer which may not have caused any problems or needed treatment.

Does testosterone replacement therapy cause heart disease?
There are some studies that suggest older men might be at risk of heart problems if given testosterone, particularly if they already have heart disease or are at high risk of heart disease. However other studies have not shown such risks, and some have shown a reduced risk in men prescribed testosterone, so the evidence is not conclusive. As a precaution, older men with heart disease or risk factors for heart disease should have these treated before starting testosterone treatment.

Where do I go for more information and support?

For information

- Visit your doctor (GP)
- Find an Endocrinologist: http://www.hormonesaustralia.org.au/find-an-endocrinologist/
- Visit Healthy Male for more information about low testosterone
- Visit Healthy Male for more information about Klinefelter syndrome

For support

Treatment for androgen deficiency is very effective in reversing physical symptoms. However, the effects of hypogonadism on the male body, sex drive and fertility can sometimes be difficult to handle. This can lead to emotional problems, relationship difficulties and depression. Professional counselling can help and support you with these issues. Discuss this with your doctor, who can recommend a psychologist or counsellor.

For those affected by sex chromosome variations, including Klinefelter syndrome, see the Australian X and Y Spectrum Support. This network brings together state groups from around Australia to support individuals and families affected by Klinefelter syndrome. http://axys.org.au/

When to see your doctor

See your doctor (GP) if you think you have symptoms or signs of hypogonadism, or testosterone deficiency. Your GP can refer you to an endocrinologist – a doctor specialising in hormones and glands.

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Making the correct diagnosis is important and treatment is very effective in most cases. Some men suffer from hypogonadism or testosterone deficiency and never seek help, and so are never treated.

Questions to ask your doctor

Seeing your doctor or having a medical problem can be stressful. It often takes time for information to sink in and it is very common to feel overwhelmed by what is happening.

Sometimes it is helpful to write down questions for your doctor before you go.

Some questions that might be useful for you are:

- Do I have testosterone deficiency?
- What is the cause?
- What are my choices for medication?
- How quickly should the medicine work?
- Does my medication have any side effect?
- How long do I need to take my medicines?
- Do I need a bone mineral density scan?
- Do I need to take other hormones or medications?
- Can I father a child if I take medication?
- Do I need another appointment or to see a specialist?

Common terms and definitions

Androgen
Male sex hormones. The primary androgen in men is testosterone.

Anorchidism
Absence of one or both testes from birth.

Chromosomes
Packages of genes that are present inside every cell. Most people have 23 pairs of chromosomes (or 46 chromosomes), which includes one pair of sex chromosomes.

Gland
A part of the body that makes and releases hormones directly into the blood stream.

Glucocorticoids
A group of adrenal hormones that occur naturally; Medications such as hydrocortisone, cortisone acetate, prednisolone and dexamethasone.

Gynaecomastia
Enlarged breasts in men.

Haemochromatosis
An inherited condition where the body absorbs and stores too much iron from the gastrointestinal tract (stomach and intestines).

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Hypogonadism
Reduced activity of the gonads (testes in men, ovaries in women).

Kallmann syndrome
A genetic condition resulting from a lack of sex hormone production, so that puberty is delayed or absent.

Karyotype
The number and physical appearance of the chromosomes in a cell. This test is performed to assist in determining if an individual has any changes in their chromosome structure, as these can cause problems with the body's functions.

Klinefelter syndrome
A condition where men are born with an extra X chromosome. This means instead of having the typical XY sex chromosomes, men have an XXY sex chromosome arrangement.

Libido
Interest in sex; sex drive.

Opioid
A group of drugs that relieve pain and relax the body.

Prader-Willi syndrome
A genetic disorder with many symptoms including abnormal growth and body composition, obesity, muscle weakness, intellectual disability and delayed puberty due to an underlying hormone deficiency.

Prolactinoma
Tumour in the pituitary gland which produces high levels of the hormone prolactin.

Prostate Specific Antigen (PSA)
A protein made by the prostate gland.

Sex Hormone Binding Globulin (SHBG)
A protein that binds to, and then carries, sex hormones through the blood.

Tumour
An abnormal growth in the body. Tumours can be benign or malignant.

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About this factsheet

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