

## What is hypogonadism in men?



Hypogonadism in men describes a condition where the testes are unable to produce enough testosterone (called androgen deficiency) and/or a normal number of sperm.

Because 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.

The loss of sperm production results in infertility (an inability to naturally father children).

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<sup>1</sup>. Other causes are less common.

Older men as a group tend to have lower testosterone concentrations compared with younger men<sup>2</sup>. 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. This is very different from the gradual decline in testosterone that occurs in some men over time<sup>3</sup>. The use of these terms in reference to men is misleading, and often used to promote testosterone therapy for reasons other than hypogonadism, where there is no evidence of benefit.

Further, recent research suggests that some men might not experience a fall in testosterone as they age<sup>4</sup>. 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<sup>5</sup>. In these men, a low testosterone level may be a marker for general poor health<sup>6</sup>. The best way to maintain testosterone levels during the transition from middle to older age may be to engage in healthy lifestyle behaviours<sup>7</sup> and avoid excess weight gain<sup>8, 9</sup>.

## What causes hypogonadism in men?

**Primary hypogonadism:** Primary hypogonadism results from conditions affecting the testes, resulting in androgen deficiency and reduced fertility<sup>10</sup>. This includes:

- Undescended testes
- Absent testes (anorchidism)
- Infections (e.g. mumps)
- Testicular injuries
- Tumours
- Cancer treatment (chemotherapy or radiotherapy to the testes)
- Genetic conditions such as Klinefelter’s syndrome.

**Secondary hypogonadism:** Secondary hypogonadism is caused by conditions that affect the hypothalamus and/or the pituitary gland<sup>10</sup>. In these cases, the testes do not receive the signals to make testosterone and sperm. This is because the hypothalamus and pituitary gland don’t make enough of the hormones that signal the testes (such as from the hypothalamus, and luteinising hormone (LH), or follicle stimulating hormone (FSH), from the pituitary gland).

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

- Tumours (and their treatments)
- Genetic conditions, e.g. Kallmann’s syndrome, Prader-Willi syndrome, hemochromatosis

### Other causes of reduced 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 androgen deficiency.

**Weight:** Men who are overweight can have lower levels of testosterone in the blood, also in the absence of any disorders of the hypothalamus, pituitary or testes.

#### Other health conditions and medications:

There are conditions that cause reduced function of the hypothalamus and pituitary gland. This can include other diseases in the body and mental health disorders such as depression. Some medications, such as glucocorticoids and opioids, 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.

**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 and sexual problems. These effects are usually reversible after stopping anabolic steroid use, although the recovery time appears to depend on the length of time and dose they were taken<sup>11</sup>.

### What are the symptoms and signs of hypogonadism?

Hypogonadism results in androgen deficiency and loss of sperm production.

The symptoms and signs of androgen 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.

Symptoms and signs of androgen deficiency by age:

**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<sup>10</sup>. 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

### How is androgen deficiency diagnosed?

A series of tests are required to carefully diagnose the cause of hypogonadism<sup>10, 12</sup>. 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)
- 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 androgen 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's syndrome).

## 2. Testosterone measurement

If symptoms and signs suggest hypogonadism or androgen deficiency, the next test your doctor might choose to do is 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<sup>10</sup>.

### **What do the results mean?**

- **Normal testosterone and LH/FSH levels** – androgen deficiency is very unlikely. Your doctor may conduct other tests to identify the cause of your symptoms.
- **Low testosterone and high LH/FSH** – suggests hypogonadism or androgen deficiency due to a testicular disorder. Further investigations will be performed to diagnose the cause.
- **Low testosterone and low or normal LH/FSH** – suggests hypogonadism or androgen deficiency due to a disorder of the hypothalamus or pituitary. Further investigations will be performed to diagnose a cause.

## 3. Additional blood and genetic testing

These tests may be conducted to identify the cause of low testosterone<sup>10</sup>. 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 hemochromatosis – a genetic condition resulting in high iron levels, which can affect pituitary function.
- **Karyotyping.** This is used to assess the number, size and shape of the chromosomes to check for genetic conditions (such as Klinefelter's 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. 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.

### ***What do the results mean?***

Results are generally reported as a T score, relative to young people of the same sex.

- T-scores above -1.0 indicate normal bone density.
- T scores between -1.0 and -2.5 indicate osteopenia (lower than expected bone density).
- T scores below -2.5 indicate osteoporosis (low bone density and increased risk of bone fractures).

## How is hypogonadism treated?

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

### **Fertility**

If a man with hypogonadism wants to father a child, this needs to be assessed. Treatment for reduced fertility temporarily takes precedence over testosterone treatment. It is very important to understand testosterone treatment does not improve fertility. In fact, testosterone treatment may reduce sperm count and reduce the chance to father a child. However, men may still be fertile while taking testosterone, so contraception/protection is still needed if they do not wish to have a baby.

### **Androgen deficiency**

For men with androgen deficiency due to hypothalamic, pituitary or testicular disorders, testosterone replacement therapy is usually indicated. The main goal of this treatment is to improve symptoms, as these can vary between men.

In Australia, there are three main ways to receive testosterone replacement therapy<sup>12</sup>.

1. **Testosterone gel or cream** – applied daily onto the skin.
2. **Testosterone injections** – into the gluteal muscle by a health care professional administered every 3 months.
3. **Oral capsules** – taken 2-3 times per day (although this option is usually less effective for most men).

Care must be taken to cover the skin after using gel or cream. This is to avoid accidentally transferring the testosterone to other people, particularly those you have close physical contact with (e.g. partner, children, carer).

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 is uncommon but may occur. Giving testosterone treatment reduces sperm count and impairs 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 treatment).

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 bone health. Prostate examinations 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.

## 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 hemochromatosis.

### ***How long do I have to take my medication?***

In most cases, testosterone replacement therapy for men with androgen 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 with testosterone replacement therapy are monitored closely by their doctors. This often includes prostate checks. This means there is an increased 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 to go for more information and support?***

#### **For information...**

Visit your doctor (GP)

Find an Endocrinologist: <http://www.hormones-australia.org.au/find-an-endocrinologist/>

Healthy Male for information about low testosterone: <https://www.healthymale.org.au/mens-health/testosterone-deficiency>

Healthy Male for information about Klinefelter's syndrome: <https://www.healthymale.org.au/mens-health/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 androgen deficiency. Your GP can refer you to an endocrinologist – a doctor specialising in hormones and glands.

Making the correct diagnosis is important and treatment is very effective in most cases. Some men suffer from hypogonadism or androgen 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 androgen 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

**Adenoma** – a non-cancerous tumour located in a gland

**Androgen** – male sex hormones. The primary androgen in men is testosterone

**Anorchidism** – absence of one or both testes from birth

**Apnoea** – condition where breathing temporarily stops during sleep

**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

**Hemochromatosis** – an inherited condition where the body absorbs and stores too much iron from the gastrointestinal tract (stomach and intestines).

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

**Hypergonadotrophic** – increased levels of hormones that stimulate the gonads (testes in men, ovaries in women).

**Kallmann's 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** – a non-cancerous 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 swelling or growth in the body. Can be benign (harmless) or malignant (cancerous)

## References

1. Herlihy AS, Halliday JL, Cock ML, McLachlan RI. The prevalence and diagnosis rates of

- Klinefelter syndrome: an Australian comparison. *Med J Aust.* 2011;194(1):24-28.
2. Yeap BB, Alfonso H, Chubb SA, Handelsman DJ, Hankey GJ, Norman PE, et al. Reference ranges and determinants of testosterone, dihydrotestosterone, and estradiol levels measured using liquid chromatography-tandem mass spectrometry in a population-based cohort of older men. *J Clin Endocrinol Metab.* 2012;97(11):4030-4039.
  3. Saad F, Gooren LJ. Late onset hypogonadism of men is not equivalent to the menopause. *Maturitas.* 2014;79(1):52-57.
  4. Sartorius G, Spasevska S, Idan A, Turner L, Forbes E, Zamojska A, et al. Serum testosterone, dihydrotestosterone and estradiol concentrations in older men self-reporting very good health: the healthy man study. *Clin Endocrinol (Oxf).* 2012;77(5):755-763.
  5. Watts EL, Appleby PN, Albanes D, Black A, Chan JM, Chen C, et al. Circulating sex hormones in relation to anthropometric, sociodemographic and behavioural factors in an international dataset of 12,300 men. *PLoS One.* 2017;12(12):e0187741.
  6. Grossmann M, Matsumoto AM. A Perspective on Middle-Aged and Older Men With Functional Hypogonadism: Focus on Holistic Management. *J Clin Endocrinol Metab.* 2017;102(3):1067-1075.
  7. Yeap BB, Almeida OP, Hyde Z, Norman PE, Chubb SA, Jamrozik K, et al. Healthier lifestyle predicts higher circulating testosterone in older men: the Health In Men Study. *Clin Endocrinol (Oxf).* 2009;70(3):455-463.
  8. Camacho EM, Huhtaniemi IT, O'Neill TW, Finn JD, Pye SR, Lee DM, et al. Age-associated changes in hypothalamic-pituitary-testicular function in middle-aged and older men are modified by weight change and lifestyle factors: longitudinal results from the European Male Ageing Study. *Eur J Endocrinol.* 2013;168(3):445-455.
  9. Shi Z, Araujo AB, Martin S, O'Loughlin P, Wittert GA. Longitudinal changes in testosterone over five years in community-dwelling men. *J Clin Endocrinol Metab.* 2013;98(8):3289-3297.
  10. Yeap BB, Grossmann M, McLachlan RI, Handelsman DJ, Wittert GA, Conway AJ, et al. Endocrine Society of Australia position statement on male hypogonadism (part 1): assessment and indications for testosterone therapy. *Med J Aust.* 2016;205(4):173-178.
  11. Handelsman DJ. Androgen misuse and abuse. *Best Pract Res Clin Endocrinol Metab.* 2011;25(2):377-389.
  12. Yeap BB, Grossmann M, McLachlan RI, Handelsman DJ, Wittert GA, Conway AJ, et al. Endocrine Society of Australia position statement on male hypogonadism (part 2): treatment and therapeutic considerations. *Med J Aust.* 2016;205(5):228-231.

## About this fact sheet

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