



Male Hypogonadism

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This leaflet is part of EAU Patient Information on male hypogonadism. It contains general information about this condition. If you have any specific questions about your individual medical situation you should consult your doctor or other professional healthcare provider. No leaflet can replace a personal conversation with your doctor.

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Male hypogonadism

What is male hypogonadism?

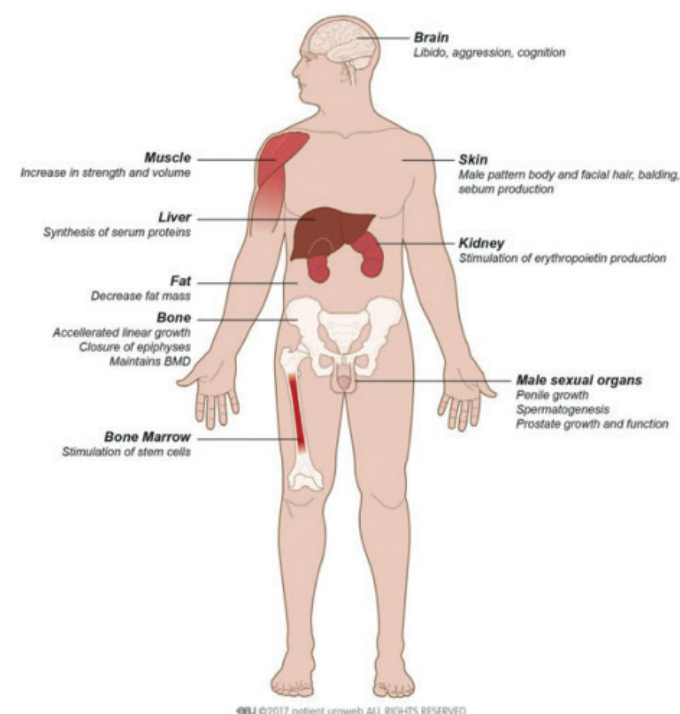
Male hypogonadism means the testicles do not produce enough of the male sex hormone testosterone. When levels are low, men might have decreased sex drive, less muscle mass, erectile dysfunction, and fatigue.

Hypogonadism has a negative effect on organ function and quality of life. Testosterone is responsible for male reproductive and sexual functions. It affects puberty, fertility, muscle mass, body composition, bone strength, fat metabolism, sex drive, mood and mental processes (Fig. 1).

Testosterone is an androgen. Production of androgens decreases slightly with age. Low levels are more common in men who are obese and have multiple health conditions.

Hypogonadism in childhood

Hypogonadism can develop at any age but affects young children, adolescent boys, and men differently. It has little impact on young children and may well go away over time.



1: Testosterone target organs.

In contrast, low hormone levels at puberty can affect a boy's sexual development.

Adolescent boys with hypogonadism typically have undeveloped muscles and genitals, a high-pitched voice, and little or no body hair. Breasts may form, and arms and legs may become out of proportion to a small torso as they continue to grow.

In most cases, a delay in development is normal and will correct itself, although the wait may be emotionally and socially difficult.

Check for hypogonadism if a boy:

- Shows symptoms of hypogonadism
- Has male family members who had hypogonadism
- Has hormone levels that decrease
- Has had injuries, infections, or medical treatments that can affect hormone levels

Living with hypogonadism

For most adults with hypogonadism, the condition is lifelong and treatment is ongoing. The goal is to improve quality of life, sense of well-being, sexual function, and muscle and bone strength. Hormone replacement combined with weight loss, a healthy diet, stopping smoking, and increasing exercise can help.

Symptoms of hypogonadism

Hypogonadism can occur at any age. The symptoms will be different depending on your age when it develops.

Common symptoms in adult men include:

- Fatigue
- Hot flashes
- Low sex drive
- Erectile dysfunction
- Mood changes
- Difficulty concentrating
- Problems sleeping
- Loss of muscle mass
- Decreased bone density
- Enlarged breasts
- Loss of body hair
- Infertility

Older men with low hormone levels may have low sexual desire and activity, erectile dysfunction, and hot flushes. In men with normal testosterone levels, these symptoms can be caused by other conditions.

Diagnosis of hypogonadism

Male hypogonadism is diagnosed based on:

- Long-term discomfort from symptoms
- Low testosterone levels in the blood measured at least two separate times

Your doctor might refer you to a hormone specialist (endocrinologist) if hypogonadism is suspected.

Various symptoms that you may have are presented below.

Physical and clinical symptoms suggestive of low testosterone:

- Small testes
- Male infertility
- Little body hair
- Gynaecomastia – enlarged breast tissue in men
- Decrease in body mass and muscle strength
- Central obesity
- Metabolic syndrome (having three of the five following conditions: central obesity, high blood pressure, high blood sugar, high blood triglycerides, and low blood high-density lipoprotein (HDL))
- Type 2 diabetes
- Osteoporosis (small bone density)
- Mild anaemia

Sexual symptoms suggestive of low testosterone:

- Reduced sexual desire and sexual activity
- Erectile dysfunction
- Fewer and smaller early morning erections

Perception symptoms suggestive of low testosterone:

- Hot flushes
- Changes in mood, fatigue and anger
- Sleep disturbances
- Depression
- Smaller perception function

Physical examination

A physical exam will look at your body hair, male pattern hair loss, body mass index, the waist-hip ratio, muscle mass,

presence of gynaecomastia, testicular size, examination of the penis and digital rectal examination of the prostate. Your doctor will make sure they are consistent with your age. Your doctor might also take a medical history to assess your general health.

For an adult patient, the doctor could also ask about your sexual life.

Blood test

If you have symptoms of hypogonadism, your doctor will take blood to test your testosterone level. Blood should be drawn in the morning before breakfast. This test should be done at least two separate times.

Additional tests

If both tests confirm you have low testosterone, further testing can determine whether the cause is testicular (primary hypogonadism) or pituitary (secondary type).

Tests to determine type of hypogonadism	
Additional blood tests	Other conditions can cause the same symptoms as hypogonadism. Bloods tests will also assess levels of: <ul style="list-style-type: none"> • Hormones produced by the <u>pituitary gland</u> (pituitary function) • Iron (anaemia) • The hormone prolactin, which causes breast growth (gynaecomastia) • Thyroid hormones (thyroid function)
Imaging	MRI or CT scan may be used to check for tumours in the pituitary gland
Genetic testing	Some types of hypogonadism are caused by problems in the way the genes developed. These tests can check for genetic causes of low hormone levels.

Treatment of hypogonadism

Losing weight, adjusting your diet, stopping smoking, and increasing exercise can improve your quality of life with hypogonadism. These changes can also help increase muscle strength and improve diabetes control and sexuality.

Hormone replacement therapy is the main treatment for both types of hypogonadism. Tumours found in the pituitary gland may require surgery, medication, radiation, or replacement of other hormones.

* The underlined terms are listed in the glossary.

Main indications for testosterone treatment:

- Delayed puberty
- Klinefelter syndrome with hypogonadism
- Sexual dysfunction and low testosterone, not responding to medication or proper medical treatment
- Osteoporosis in hypogonadism
- Adult men with low testosterone and consistent multiple symptoms of hypogonadism following unsuccessful treatment of obesity and other medical conditions
- Under-active pituitary gland (hypopituitarism)

Contra-indications against testosterone treatment:

- Advanced or metastatic prostate cancer
- Men with active desire to have children
- High level of haematocrit > 54%
- Severe cardiac failure (New York Heart Association IV)

Hormone replacement therapy

The goal of hormone replacement is to improve quality of life, sense of well-being, sexual function, muscle strength, and bone mineral density.

Replacement of the hormone testosterone aims to restore levels in men diagnosed with low testosterone caused by problems in the testicles (primary hypogonadism).

Pituitary hormones may be replaced if low levels are caused by a problem in the pituitary gland (secondary hypogonadism). These hormones can stimulate genital development in boys. They can increase sperm production and restore fertility in men.

Risks of testosterone treatment

In addition to side effects, hormone replacement carries some risks related to natural changes in hormone levels. Testosterone replacement can cause both cancerous and non-cancerous prostate tumours, enlarged breasts, infertility, and blood clots in the veins.

Do not use testosterone replacement therapy if you have:

- Heart problems
- Prostate cancer
- An enlarged prostate that causes problems urinating
- Male breast cancer
- A high red blood cell count
- Severe sleep apnoea
- Infertility but might want to have children

Types of testosterone replacement therapy

Different types of testosterone replacement are absorbed into the body differently and have different side effects.

Consider starting therapy with a type that can be stopped easily (short-acting treatment) if side effects are a problem. Not all types of testosterone replacement therapy are available. Work with your doctor to choose the right type of testosterone replacement therapy for you.

Type	Formulation	Side effects
Taken by mouth	<ul style="list-style-type: none">• Short-acting: <u>testosterone undecanoate</u> pills, sublingual testosterone (tablet placed under the tongue to dissolve) buccal testosterone tablet (swallowed)	<ul style="list-style-type: none">• Widely used with few or no side effects. Safe when used for a limited time.
Injected into the buttock or arm	<ul style="list-style-type: none">• Short-acting: <u>testosterone cypionate</u> and <u>enanthate</u> (every 2–3 weeks).• Long-acting: <u>testosterone undecanoate</u> (every 3 months)• Subdermal depot (patch placed under the skin releases medicine over 5–7 months).	<ul style="list-style-type: none">• Short-acting injections can cause testosterone levels to vary, sometimes too high and sometimes too low. This may cause symptoms to appear and disappear during treatment.• With depot there is a risk of infection or implant coming out.
Applied to the skin	<ul style="list-style-type: none">• Short-acting: <u>transdermal testosterone gel</u>.	<ul style="list-style-type: none">• Short-acting treatment can cause skin to become irritated. Medicine can be transferred accidentally to another person who comes into contact with it.

Follow-up

Regular medical monitoring is recommended during treatment. Your doctor will schedule visits with you to assess whether treatment is working, address possible side effects, and check treatment safety. Your testosterone will be tested over time to help determine the right dosage for therapy. Follow-up may include blood tests, examination of your prostate and your heart, and bone density scans.

With treatment, your symptoms will go away gradually. For example, your sex drive might improve first, then your mood might improve, and then erectile function might return.

* The underlined terms are listed in the glossary.

General information

Testosterone production

Testosterone is produced mainly in the testicles and also by the adrenal glands. Women have testosterone, but in much smaller amounts than men.

In the brain, the hypothalamus and pituitary gland help the testicles produce testosterone. They produce hormones that prompt action in the testicles. In response, the testicles produce sperm and testosterone.

What does testosterone do?	
Brain	Affects sex drive, mood, and mental processes (cognition)
Skin	Affects male pattern body and facial hair, balding, and oil production
Larynx	Deepens voice and prompts formation of Adam's apple
Organ	Stimulates production of erythropoietin, which causes red blood cells to form
Male sexual organs	Affect penile and prostate growth and function and production of sperm
Muscle	Increases strength and muscle mass
Liver	Affects production of proteins
Fat	Decreases fat mass
Bone marrow	Stimulates production of stem cells
Bone	Accelerates growth, increases bone strength, and maintains bone density

Types and causes of hypogonadism

Primary hypogonadism is caused by a problem in the testicles. Secondary hypogonadism is caused by a problem in glands that tell the testicles to make testosterone.

* The underlined terms are listed in the glossary.

Common causes of hypogonadism

Male hypogonadism of testicular origin (primary)	Male hypogonadism of hypothalamic - pituitary origin (secondary)
<p>Primary testicular failure is the most frequent cause of hypogonadism. It involves low testosterone level, incorrect sperm production and elevated gonadotropins (LH and FSH – hormones produced in pituitary to stimulate testes to work properly). The most common conditions of primary hypogonadism are Klinefelter syndrome and testicular tumours.</p> <ul style="list-style-type: none"> • Klinefelter syndrome: A set of symptoms that result from extra X chromosome in male. A set of chromosomes is called karyotype (in male it is 46, XY. In Klinefelter, in 90% of cases it is 47, XXY). It is caused by incorrect division of cells within embryo. • Testicular cancer. Risk factor is contralateral testicular cancer, undescended testes, testicular dysgenesis (incorrect structure of tissue in the testes), infertility, small testes and testicular cancer in the family. 25% of men develop hypogonadism after treatment of testicular cancer. <p>Forms of primary hypogonadism:</p> <ul style="list-style-type: none"> • Undescended testicles • Klinefelter Syndrome 47, XXY • Testicular cancer • Mumps infection involving the testicles • Loss of testes (trauma, surgical removal) • Small testes or dysgenesis • Disorders of sex development (DSD) • 46, XX male syndrome (genetic information of Y chromosome translocated to X chromosome) • Treatment for testicular cancer 	<p>Forms of secondary hypogonadism:</p> <ul style="list-style-type: none"> • Kallmann's syndrome – genetic hypogonadotrophic hypogonadism with lack of smell sensation (anosmia) • Hyperprolactinemia • Isolated or congenital hypogonadotrophic hypogonadism. Lack of GnRH. • Secondary lack of GnRH (hypothalamic hormone), due to drugs, toxins or systemic disease • Hypopituitarism (under-active pituitary gland) after radiotherapy, trauma or infections • Iron overload (haemochromatosis, thalassemia) <p>Defects of hypothalamus or pituitary cause secondary testicular failure. The most important forms are:</p> <ul style="list-style-type: none"> • Hyperprolactinemia – caused by benign tumours of the pituitary gland that produce too much of prolactin. This condition may be caused by medication (drug-induced), chronic renal failure or under-active thyroid gland. • Isolated or congenital hypogonadotrophic hypogonadism (low FSH, low LH and low testosterone of unknown origin) • Kallmann's syndrome – genetic hypogonadotrophic hypogonadism with lack of smell sensation (anosmia) <p>As pituitary secretes low levels of LH and FSH, it does not stimulate testes to secrete testosterone, there is delayed puberty.</p>
<p>* Decreased testosterone varies greatly among men. Almost a third of men older than age 75 have low testosterone.</p>	
<p>Male hypogonadism due to mixed dysfunction of hypothalamus / pituitary and testes (adult onset)</p>	<p>Male hypogonadism due to defects of androgen target organs</p>
<ul style="list-style-type: none"> • Combined primary and secondary testicular failure. There is low testosterone level with variable levels of gonadotropins LH and FSH. 	<ul style="list-style-type: none"> • Very rare forms. There is androgen receptor defect that may cause complete, partial or minimal androgen insensitivity syndrome.

Hypogonadism and fertility

Hypogonadism can reduce sperm production and cause infertility. Men who want to have children should not use testosterone replacement, but other treatment may be available.

Men with hypogonadism caused by pituitary problems (secondary type) can potentially be treated with a hormone called human chorionic gonadotrophin, or hCG. This hormone stimulates production of testosterone in the testicles. It is combined with treatment to increase production of sperm. This therapy can be used only for a limited time and should be guided by a competent specialist.

Men with hypogonadism caused by problems in the testicles (primary type) who have fertility problems need evaluation of the testicles and may require assisted reproductive technology. This technology can help couples who have not been able to conceive a child.

* The underlined terms are listed in the glossary.

Glossary of terms

Androgen

Group of steroid hormones, represented mainly by testosterone

Erectile dysfunction

The inability to get or keep an erection

Hypothalamus

Small organ at the base of the brain that links the nervous system with the endocrine system through the pituitary gland

Infertility

When a couple that has unprotected intercourse for a period of 2 years cannot conceive a baby

Mumps infection

A contagious viral infection of the salivary gland with fever, headache, and swelling of the salivary gland in the cheeks

Pituitary gland

Small endocrine gland in the brain that is connected to the hypothalamus and secretes a variety of hormones

Sex hormones

Hormones that determine the appropriate sex characteristics; testosterone is the main sex hormone in men

Sleep apnoea

Sleep disorder characterised by shallow breathing or pauses in breathing

Testicles

Male sex gland with the main function of producing sperm and androgens

Testosterone

Sex hormone produced mainly by the testicles that stimulates the development of sex organs and takes part in proper maintenance of muscle, bone, brain, and other organs in men

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