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**Spermatogenesis**, the origin and development of the [sperm cells](https://www.britannica.com/science/sperm) within the male [reproductive](https://www.britannica.com/science/human-reproductive-system) organs, the [testes](https://www.britannica.com/science/testis). The testes are composed of numerous thin, tightly coiled tubules known as the [seminiferous tubules;](https://www.britannica.com/science/seminiferous-tubule) the sperm cells are produced within the walls of the tubules. Within the walls of the tubules, also, are many randomly scattered cells, called [Sertoli cells](https://www.britannica.com/science/Sertoli-cell), that function to support and nourish the immature sperm cells by giving them nutrients and blood products. As the young germ cells grow, the Sertoli cells help to transport them from the outer surface of the seminiferous tubule to the central channel of the tubule.



[](https://www.britannica.com/science/testis%22%20%5Cl%20%22ref1096284)

[The seminiferous tubules, in which the sperm are produced, constitute about 90 percent of the testicular mass. In the young male the tubules…](https://www.britannica.com/science/testis%22%20%5Cl%20%22ref1096284)

Sperm cells are continually being produced by the testes, but not all areas of the seminiferous tubules produce sperm cells at the same time. One immature germ [cell](https://www.britannica.com/science/cell-biology) takes as long as 74 days to reach final maturation, and during this growth process there are [intermittent](https://www.merriam-webster.com/dictionary/intermittent) resting phases.

The immature cells (called [spermatogonia](https://www.britannica.com/science/spermatogonium)) are all derived from cells called [stem cells](https://www.britannica.com/science/stem-cell) in the outer wall of the seminiferous tubules. The stem cells are composed almost entirely of nuclear material. (The nucleus of the cell is the portion containing the chromosomes.) The stem cells begin their process by multiplying in the process of cell duplication known as [mitosis](https://www.britannica.com/science/mitosis). Half of the new cells from this initial crop go on to become the future sperm cells, and the other half remain as stem cells so that there is a constant source of additional germ cells. Spermatogonia destined to develop into mature sperm cells are known as primary sperm cells. These move from the outer portion of the seminiferous tubule to a more central location and attach themselves around the Sertoli cells. The primary sperm cells then develop somewhat by increasing the amount of [cytoplasm](https://www.britannica.com/science/cytoplasm) (substances outside of the nucleus) and structures called organelles within the cytoplasm. After a resting phase the primary cells [divide into a form](https://www.britannica.com/science/meiosis-cytology) called a secondary sperm cell. During this [cell division](https://www.britannica.com/science/cell-division) there is a splitting of the nuclear material. In the nucleus of the primary sperm cells there are 46 chromosomes; in each of the secondary sperm cells there are only 23 chromosomes, as there are in the egg. When the egg and sperm combine and their chromosomes unite, the characteristics of both individuals blend and the new organism starts to grow.

The secondary sperm cell still must mature before it can fertilize an egg; maturation entails certain changes in the shape and form of the sperm cell. The nuclear material becomes more condensed and oval in shape; this area develops as the head of the sperm. The head is covered partially by a cap, called the acrosome, which is important in helping the sperm to gain entry into the egg. Attached to the opposite end of the head is the tailpiece. The tail is derived from the secondary sperm cell’s cytoplasm. In the mature sperm, it consists of a long, slender bundle of filaments that propel the sperm by their undulating movement. Once the sperm has matured, it is transported through the long seminiferous tubules and stored in the [epididymis](https://www.britannica.com/science/epididyme) of the testes until it is ready to leave the male body.

2.TESTERONE;

Testosterone is the primary male hormone responsible for regulating sex differentiation, producing male sex characteristics, spermatogenesis and fertility. Testosterone’s effects are first seen in the fetus. During the first 6 weeks of development, the reproductive tissues of males and females are identical. At around week 7 in utero, the SRY (sex-related gene on the Y chromosome) initiates the development of the testicles. Sertoli cells from the testis cords (fetal testicles) eventually develop into seminiferous tubules. Sertoli cells produce a Mullerian-inhibiting substance (MIS), which leads to the regression of the fallopian tubes, uterus, and upper segment of the vagina (Mullerian structures normally present in females). Fetal Leydig cells and endothelial cells migrate into the gonad and produce testosterone, which supports the differentiation of the Wolffian duct (paramesonephric duct) structures that go on to become the male urogenital tract. Testosterone also gets converted to dihydrotestosterone (DHT) in the periphery (discussed below) and induces the formation of the prostate and male external genitalia. Testosterone is also responsible for testicular descent through the inguinal canal, which occurs in the last 2 months of fetal development. When an embryo lacks a Y chromosome and thus the SRY gene, ovaries develop. Fetal ovaries do not produce adequate amounts of testosterone, thus the Wolffian ducts do not develop. There is also an absence of MIS in these individuals, leading to the development of the Mullerian ducts and female reproductive structures.

**Function**

Testosterone is responsible for the development of primary sexual development, which includes testicular descent, spermatogenesis, enlargement of the penis and testes, and increasing libido. The testes usually begin the descent into the scrotum around 7 months of gestation, when the testes begin secreting reasonable quantities of testosterone. If a male child is born with undescended but normal testes that do not descend by 4 to 6 months of age, administration of testosterone can help the testes descend through the inguinal canals.

Testosterone is also involved in regulating secondary male characteristics, which are those responsible for masculinity. These secondary sex characteristics include male hair patterns, vocal changes, and voice deepening, anabolic effects which include growth spurts in puberty (testosterone increases tissue growth at the epiphyseal plate early on and eventual closure of plate later in puberty) and skeletal muscle growth (testosterone stimulates protein synthesis). Testosterone also stimulates erythropoiesis, which results in a higher hematocrit in males versus females. Testosterone levels tend to drop with increasing age; because of this, men tend to experience a decrease in testicular size, a drop in libido, lower bone density, muscle mass decline, increased fat production, and decreased erythropoiesis which leads to possible anemia.

**Mechanism**

In puberty, the hypothalamic-pituitary-gonadal axis takes a major role in regulating testosterone levels and gonadal function. The hypothalamus secretes GnRH, which travels down the hypothalamo-hypophyseal portal system to the anterior pituitary, which secretes luteinizing hormone (LH) and follicle stimulating hormone (FSH). LH and FSH are two gonadotropic hormones which travel through the blood and act on receptors in the gonads. LH in particular acts on the Leydig cells to increase testosterone production. Testosterone limits its own secretion via negative feedback. High levels of testosterone in the blood feedback to the hypothalamus to suppress the secretion of GnRH and also feedback to the anterior pituitary, making it less responsive to GnRH stimuli.

Throughout the reproductive life of males, the hypothalamus releases GnRH in pulses every 1 to 3 hours. Despite this pulsatile release, however, average plasma levels of FSH and LH remain fairly constant from the start of puberty, where levels spike, to the third decade of life, where levels peak and slowly begin to decline. Prior to puberty, testosterone levels are low, reflecting the low secretion of GnRH and gonadotropins. Changes in neuronal input to the hypothalamus and brain activity during puberty, cause a dramatic rise in GnRH secretion.

Leydig cells in the testes function to turn cholesterol into testosterone. LH regulates the initial step in this process. Two important intermediates in this process are dehydroepiandrosterone (DHEA) and androstenedione. Androstenedione is converted to testosterone by the enzyme 17-beta-hydroxysteroid dehydrogenase. The majority of testosterone is bound to plasma proteins such as sex-hormone-binding-globulin and albumin. This majority supply of protein-bound testosterone acts as a surplus of testosterone hormone for the body. The small amounts of free testosterone in the blood act at the level of the tissues, primarily the seminal vesicles, bone, muscle, and prostate gland. At the cellular level, testosterone gets converted to dihydrotestosterone by the enzyme 5-alpha-reductase. Testosterone and dihydrotestosterone can bind to cell receptors and regulate protein expression. Both men and women also produce weak acting androgens in the zona reticularis of the adrenal glands. These weak-acting androgens are known as dehydroepiandrosterone and androstenedione. They bind to testosterone receptors with weaker affinity but can also be converted to testosterone in the peripheral tissues if produced at high amounts.

**Related Testing**

Features of testosterone deficiency can be very apparent, which is why the first steps in diagnosing male hypogonadism involve adequate history taking and physical exam. The features indicative of male hypogonadism can be divided into pre and post-pubertal. Pre-pubertal features include small testes (less than 20 mL in volume), small phallus, decreased secondary sex characteristics (e.g., facial or axillary hair), gynecomastia, difficulty gaining muscle mass, eunuchoid proportions, low sperm count, and low energy/libido. Post-pubertal features include those previously mentioned (except phallus size and eunuchoid proportions) as well as osteoporosis and hot flashes with severe hypogonadism.

If a clinician expects hypogonadism based on history and physical, a total serum testosterone between 8 AM and 10 AM should be drawn. Normal levels may indicate eugonadal low testosterone. If levels are low, a repeat level should be obtained along with FSH and LH levels. Low testosterone in the setting of normal FSH/LH indicates secondary hypogonadism. The next steps would be to get prolactin, T4, 8 AM cortisol, iron, and ferritin levels as well as brain MRI. Low testosterone in the setting of elevated FSH/LH indicated primary hypogonadism. In the case of primary hypogonadism, a karyotype should be established.

Hyperandrogenism also has various clinical presentations, depending on puberty status and gender. Prepubertal boys with hyperandrogenism may present with virilization. Virilization includes penile enlargement, excess hair growth in androgen-dependent areas, and voice deepening. In prepubertal girls, hyperandrogenism may lead to clitoromegaly, acne, and hirsutism. In adult males, the effects of excess testosterone depend on whether the source is from the adrenals or exogenous. Adrenal androgen elevations have few observable effects in males and do not cause an increase in muscle mass or hair growth. In adult females, increased adrenal androgens can lead to acne, hirsutism, menstrual irregularities, infertility, male-pattern baldness, or virilization.

Testosterone can be used to treat and manage various medical conditions. Medical conditions in which testosterone can be used include metastatic breast cancer, delayed puberty, hypogonadotropic hypogonadism (congenital or acquired), and primary hypogonadism. Toxic effects of testosterone and synthetic androgens include over-masculinization, hirsutism, decreased menses, acne, and clitoral enlargement. Rarely, synthetic androgens can cause hepatic adenoma, cholestatic jaundice, and prostatic hypertrophy. Synthetic androgens and testosterone are contraindicated in pregnancy.

Androgen antagonists come in different types. GnRH analogs, if given continuously, can act as medical castration drugs and are used in treating prostate cancer. Androgen receptor inhibitors, like flutamide and spironolactone, can be used for patients with hirsutism. Steroid synthesis inhibitors, like ketoconazole, can be used in Cushing disease. 5-alpha reductase inhibitors, like finasteride, can be used to treat benign prostatic hyperplasia.

**Clinical Significance**

Pathology related to testosterone involves either over-production, under-production, receptor insensitivity, or impaired metabolism of testosterone. The following are a few of the more common and highly tested testosterone pathologies.

Over-production of androgens can occur in the following conditions: polycystic ovarian syndrome (PCOS), adrenal virilization/adrenal tumors, ovarian or testicular tumors, Cushing syndrome, and as a result of exogenous steroid use. To better understand some of these pathologies it is important to note the differences between testosterone and dehydroepiandrosterone (DHEA). DHEA is a relatively weak androgen produced by the adrenals and ovaries/testes. DHEA serves as a precursor for other hormones including testosterone and estrogen. The sulfated form of DHEA, DHEAS, is specific for the adrenal glands. In polycystic ovary syndrome (PCOS), abnormal gonadotropin-releasing hormone (GnRH) secretion leads to an increase in LH secretion. LH stimulates androgen production by ovarian theca cells which leads to hirsutism, male escutcheon, acne and androgenic alopecia in women affected with PCOS.[[6]](https://www.ncbi.nlm.nih.gov/books/NBK526128/) In adrenal and ovarian tumors, there is usually rapidly progressing androgenic symptoms (hirsutism, virilization). If testosterone is elevated and DHEAS is normal, this is most likely from an ovarian tumor. If DHEAS is elevated and testosterone is relatively normal, this is most likely an adrenal tumor.

Decreased production of testosterone can occur with aging, certain medications, chemotherapy, hypothalamus-pituitary axis disorders, primary hypogonadism, cryptorchidism and orchitis, and with genetic disorders such as Klinefelter and Kallmann syndrome. Klinefelter syndrome is the most common congenital abnormality that results in primary hypogonadism. In Klinefelter, there is dysgenesis of seminiferous tubules and loss of Sertoli cells which leads to a decrease in inhibin levels and a resultant increase in FSH. FSH upregulates aromatase leading to increased conversion of androgens to estrogens. In Klinefelter, there is also Leydig cell dysfunction which leads to decreased testosterone levels and an increase in LH due to loss of negative feedback. In Kallmann syndrome, failed migration of GnRH-producing neurons leads to lack of GnRH. No GnRH results in a decrease in LH, FSH, testosterone, and sperm count. Specific to Kallmann syndrome, in comparison to other causes of hypogonadotropic hypogonadism, is defects in the sensation of smell (hyposmia or anosmia).

5-alpha reductase is an enzyme that converts testosterone to dihydrotestosterone. Male patients with 5-alpha reductase deficiency present with normal female or male genitalia or ambiguous genitalia at birth due to lack of dihydrotestosterone. These patients have a male internal urogenital tract (anti-Mullerian hormone is still present). At puberty, adolescents with this enzyme deficiency, who may have been raised as girls due to lack of secondary male characteristics, begin to develop male secondary sex characteristics and have primary amenorrhea. These patients will have normal testosterone and LH, low DHT, and an increased testosterone-to-DHT ratio. In contrast to 5-alpha reductase deficiency, androgen insensitivity is a condition in which patients lack functional androgen receptors resulting in under-virilization. These patients, like those with 5-alpha reductase deficiency, have a 46 XY karyotype. In contrast, however, these patients have normal female external genitalia and usually undescended testes. In adolescence, they experience primary amenorrhea and breast development but have no pubic or axillary hair and lack the deepening voice changes that occur with puberty. They will have a blind vaginal pouch and abnormal internal reproductive organs (fallopian tubes, uterus, and the upper portion of the vagina) due to the production of the Mullerian inhibiting factor. These patients will have high levels of testosterone and LH.

Impaired testosterone metabolism can occur in certain cases of congenital adrenal hyperplasia (CAH). In classic CAH (95% of cases), due to 21 hydroxylase deficiency, newborns usually present with ambiguous genitalia and later develop salt wasting, vomiting, hypotension, and acidosis. A marked increase in 17-hydroxyprogesterone is diverted towards adrenal androgen synthesis and leads to hyperandrogenism. Hyperandrogenism impairs hypothalamic sensitivity to progesterone leading to a rapid rise in GnRH synthesis and thus increased LH and FSH. Elevations in LH and FSH lead to increased gonadal steroid production (17-hydroxyprogesterone, DHEA, testosterone, LH, and FSH). Diagnosis is with adrenocorticotropic hormone stimulation test showing exaggerated 17 hydroxyprogesterone response.

## DISORDER;

Male hypogonadism is a condition in which the body does not produce enough of the testosterone hormone; the hormone that plays a key role in masculine growth and development during puberty. There is a clear need to increase the awareness of hypogonadism throughout the medical profession, especially in primary care physicians who are usually the first port of call for the patient. Hypogonadism can significantly reduce the quality of life and has resulted in the loss of livelihood and separation of couples, leading to divorce. It is also important for doctors to recognize that testosterone is not just a sex hormone. There is an important research being published to demonstrate that testosterone may have key actions on metabolism, on the vasculature, and on brain function, in addition to its well-known effects on bone and body composition. This article has been used as an introduction for the need to develop sensitive and reliable assays for sex hormones and for symptoms and treatment of hypogonadism.

## INTRODUCTION

Hypogonadism is a medical term for decreased functional activity of the gonads. The gonads (ovaries or testes) produce hormones (testosterone, estradiol, antimullerian hormone, progesterone, inhibin B, activin) and gametes (eggs or sperm).[[1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref1)] Male hypogonadism is characterized by a deficiency in testosterone – a critical hormone for sexual, cognitive, and body function and development. Clinically low testosterone levels can lead to the absence of secondary sex characteristics, infertility, muscle wasting, and other abnormalities. Low testosterone levels may be due to testicular, hypothalamic, or pituitary abnormalities. In individuals who also present with clinical signs and symptoms, clinical guidelines recommend treatment with testosterone replacement therapy.

## CLASSIFICATION OF MALE HYPOGONADISM

There are two basic types of hypogonadism that exist:

Primary: This type of hypogonadism – also known as primary testicular failure – originates from a problem in the testicles.

Secondary: This type of hypogonadism indicates a problem in the hypothalamus or the pituitary gland – parts of the brain that signal the testicles to produce testosterone. The hypothalamus produces the gonadotropin releasing hormone, which signals the pituitary gland to make the follicle-stimulating hormone (FSH) and luteinizing hormone. The luteinizing hormone then signals the testes to produce testosterone. Either type of hypogonadism may be caused by an inherited (congenital) trait or something that happens later in life (acquired), such as an injury or an infection.

### Primary Hypogonadism

Common causes of primary hypogonadism include:

Klinefelter's Syndrome: This condition results from a congenital abnormality of the sex chromosomes, X and Y. A male normally has one X and one Y chromosome. In Klinefelter's syndrome, two or more X chromosomes are present in addition to one Y chromosome. The Y chromosome contains the genetic material that determines the sex of a child and the related development. The extra X chromosome that occurs in Klinefelter's syndrome causes abnormal development of the testicles, which in turn results in the underproduction of testosterone.

### Undescended testicles

Before birth, the testicles develop inside the abdomen and normally move down into their permanent place in the scrotum. Sometimes, one or both of the testicles may not descend at birth. This condition often corrects itself within the first few years of life without treatment. If not corrected in early childhood, it may lead to malfunction of the testicles and reduced production of testosterone.

### Mumps orchitis

If a mumps infection involving the testicles in addition to the salivary glands (mumps orchitis) occurs during adolescence or adulthood, long-term testicular damage may occur. This may affect normal testicular function and testosterone production.

### Hemochromatosis

Too much iron in the blood can cause testicular failure or pituitary gland dysfunction, affecting testosterone production.

### Injury to the Testicles

Because of their location outside the abdomen, the testicles are prone to injury. Damage to normally developed testicles can cause hypogonadism. Damage to one testicle may not impair testosterone production.

### Cancer treatment

Chemotherapy or radiation therapy for the treatment of cancer can interfere with testosterone and sperm production. The effects of both treatments are often temporary, but permanent infertility may occur. Although many men regain their fertility within a few months after the treatment ends, preserving sperm before starting cancer therapy is an option that many men consider. Howell et al. reported that hypogonadism was seen in 30% of the men with cancer and 90% of these gentlemen had germinal epithelial failure.

### Normal aging

Older men generally have lower testosterone levels than younger men do. As men age, there's a slow and continuous decrease in testosterone production. The rate that testosterone declines varies greatly among men. As many as 30% of men older than 75 have a testosterone level that is below normal, according to the American Association of Clinical Endocrinologists. Whether or not treatment is necessary remains a matter of debate.[[3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref3)]

### Secondary Hypogonadism

In secondary hypogonadism, the testicles are normal, but function improperly due to a problem with the pituitary or hypothalamus. A number of conditions can cause secondary hypogonadism, including:

### Kallmann syndrome

Abnormal development of the hypothalamus – the area of the brain that controls the secretion of pituitary hormones – can cause hypogonadism. This abnormality is also associated with the impaired development of the ability to smell (anosmia).

### Pituitary disorders

An abnormality in the pituitary gland can impair the release of hormones from the pituitary gland to the testicles, affecting normal testosterone production. A pituitary tumor or other type of brain tumor located near the pituitary gland may cause testosterone or other hormone deficiencies. Also, the treatment for a brain tumor such as surgery or radiation therapy may impair pituitary function and cause hypogonadism.

### Inflammatory disease

Certain inflammatory diseases such as sarcoidosis, Histiocytosis, and tuberculosis involve the hypothalmus and pituitary gland and can affect testosterone production, causing hypogonadism.

### HIV/AIDS

This virus can cause low levels of testosterone by affecting the hypothalamus, the pituitary, and the testes.

### Medications

The use of certain drugs, such as, opiate pain medications and some hormones, can affect testosterone production.[[4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref4)]

### Obesity

Being significantly overweight at any age may be linked to hypogonadism.

### Stress-induced Hypogonadism

Stress, excessive physical activity, and weight loss have all been associated with hypogonadism. Some have attributed this to stress-induced hypercortisolism, which would suppress hypothalamic function.

## ROLE OF TESTOSTERONE

Throughout the male lifespan, testosterone plays a critical role in sexual, cognitive, and body development. During fetal development, testosterone aids in the determination of sex. The most visible effects of rising testosterone levels begin in the prepubertal stage. During this time, body odor develops, oiliness of the skin and hair increase, acne develops, accelerated growth spurts occur, and pubic, early facial, and axillary hair grows. In men, the pubertal effects include enlargement of the sebaceous glands, penis enlargement, increased libido, increased frequency of erections, increased muscle mass, deepening of voice, increased height, bone maturations, loss of scalp hair, and growth of facial, chest, leg, and axillary hair. Even as adults, the effects of testosterone are visible as libido, penile erections, aggression, and mental and physical energy.

### Pathophysiology of Testosterone and Hypogonadism

The cerebral cortex – the layer of the brain often referred to as the gray matter – is the most highly developed portion of the human brain. This portion of the brain, encompassing about two-thirds of the brain mass, is responsible for the information processing in the brain. It is within this portion of the brain that testosterone production begins. The cerebral cortex signals the hypothalamus to stimulate production of testosterone. To do this, the hypothalamus releases the gonadotropin-releasing hormone in a pulsatile fashion, which stimulates the pituitary gland – the portion of the brain responsible for hormones involved in the regulation of growth, thyroid function, blood pressure, and other essential body functions. Once stimulated by the gonadotropin-releasing hormone, the pituitary gland produces the follicle-stimulating hormone and the luteinizing hormone. Once released into the bloodstream, the luteinizing hormone triggers activity in the Leydig cells in the testes. In the Leydig cells, cholesterol is converted to testosterone. When the testosterone levels are sufficient, the pituitary gland slows the release of the luteinizing hormone via a negative feedback mechanism, thereby, slowing testosterone production. With such a complex process, many potential problems can lead to low testosterone levels. Any changes in the testicles, hypothalamus or pituitary gland can result in hypogonadism. Such changes can be congenital or acquired, temporary, or permanent.

Recent studies have found that testosterone production slowly decreases as a result of aging, although the rate of decline varies. Unlike women who experience a rapid decline in hormone levels during menopause, men experience a slow, continuous decline over time. The Baltimore Longitudinal Study of Aging reported that approximately 20% of men in their 60s and 50% of men in their 80s are hypogonadal.[[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref6)] The New Mexico Aging Process Study showed a decrease in serum testosterone of 110 ng/dL every 10 years.[[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref7)] As hormone levels decline slowly, this type of hypogonadism is sometimes referred to as the partial androgen deficiency of the aging male (PADAM). With the growing elderly population, the incidence of PADAM may increase over the next few decades.

Regardless of the age or comorbid conditions, obesity is associated with hypogonadism. The Baltimore Longitudinal Study of Aging found that testosterone decreased by 10 ng/dL per 1-kg/m2 increase in body mass index.[[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref6)] Another study also showed reduced testosterone levels in men with increased total abdominal adiposity.[[8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref8)] The proposed causes for the effects of obesity on testosterone level include increased clearance or aromatization of testosterone in the adipose tissue and increased formation of inflammatory cytokines, which hinder the secretion of the gonadotropin-releasing hormone.[[9](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref9)] Similar to the projections for an aging population, the increasing incidence of obesity may lead to an increased incidence of secondary hypogonadism. When the risk factors of obesity and age are removed, diabetes mellitus still remains an independent risk factor for hypogonadism. Although diabetes mellitus–related hypogonadism was previously thought to be associated with testicular failure, study results show one-third of diabetic men had low testosterone levels, but also had low pituitary hormone levels.[[10](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref10)] Population projections expect the number of cases of diabetes mellitus to rise from 171 million in 2000 to 366 million in 2030.[[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255409/#ref11)] This drastic increase in cases will impact the prevalence of hypogonadism as well. Certain medications are shown to reduce testosterone production. Among the medications known to alter the hypothalamic-pituitary-gonadal axis are spironolactone, corticosteroids, ketoconazole, ethanol, anticonvulsants, immunosuppressants, opiates, psychotropic medications, and hormones.

### Symptoms

Hypogonadism is characterized by serum testosterone levels < 300 ng/dL in combination with at least one clinical sign or symptom. Signs of hypogonadism include absence or regression of secondary sex characteristics, anemia, muscle wasting, reduced bone mass or bone mineral density, oligospermia, and abdominal adiposity. Symptoms of post pubescent hypogonadism include sexual dysfunction (erectile dysfunction, reduced libido, diminished penile sensation, difficulty attaining orgasm, and reduced ejaculate), reduced energy and stamina, depressed mood, increased irritability, difficulty concentrating, changes in cholesterol levels, anemia, osteoporosis, and hot flushes. In the prepubertal male, if treatment is not initiated, signs and symptoms include sparse body hair and delayed epiphyseal closure.

### Testing

Early diagnosis and treatment can reduce risks associated with hypogonadism. Early detection in young boys can help to prevent problems due to delayed puberty. Early diagnosis in men helps protect against the development of osteoporosis and other conditions. The diagnosis of hypogonadism is based on symptoms and blood work, particularly on testosterone levels. Often the first step toward diagnosis is the Androgen Deficiency in Aging Male (ADAM) test – a 10 item questionnaire intended to identify men who exhibit signs of low testosterone. Testosterone levels vary throughout the day and are generally highest in the morning, so blood levels are typically drawn early in the morning. If low testosterone levels are confirmed, further testing is done, to identify if the cause is testicular, hypothalamic, or pituitary. These tests may include hormone testing, semen analysis, pituitary imaging, testicular biopsy, and genetic studies. Once the treatment starts, the patient may continue to have testosterone levels drawn to determine if the medication is helping to produce adequate testosterone levels.