HYPOGONADISM

A medical term which describes a diminished functional activity of the gonads – the testes and ovaries.

Related Diagnoses:
- Varicocele
- Azospermia
- Erectile dysfunction
- Obesity
- Polycystic ovary syndrome
- Anovulation
- Undescended testes
- Ejaculatory disorders
- Turner syndrome
- Klinefelter syndrome
- Kallmann syndrome
- Non-obstructive azospermia
- XX male syndrome
- Delayed ejaculation
- Amenorrhea
- Hyperprolactinemia
- Noonan syndrome
- Hypoestrogenism
- Hypoandrogenism

About Hypogonadism

Hypogonadism is a medical term which describes a diminished functional activity of the gonads – the testes and ovaries.

Hypogonadism is divided into two main categories - hypogonadotropic hypogonadism and hypergonadotropic hypogonadism.

1. Hypogonadotropic hypogonadism (HH)

Also known as secondary or central hypogonadism, as well as gonadotropin-releasing hormone deficiency or gonadotropin deficiency (GD), is a condition which is characterized by hypogonadism due to an impaired secretion of gonadotropins, including follicle-stimulating hormone (FSH) and luteinizing hormone (LH), by the pituitary gland in the brain, and in turn decreased gonadotropin levels and a resultant lack of sex steroid production.

The type of HH, based on its cause, may be classified as either primary or secondary.

**Primary HH**, also called isolated hypogonadotropic hypogonadism (IHH), is a condition that results in a small subset of cases of hypogonadotropic hypogonadism due to deficiency in or insensitivity to gonadotropin-releasing hormone (GnRH) where the function and anatomy of the anterior pituitary is otherwise normal and secondary causes of HH are not present.

It presents as hypogonadism (e.g., reduced or absent puberty, low libido, infertility, etc.) due to an impaired release of the gonadotropins, follicle-stimulating hormone and luteinizing hormone, and a resultant lack of sex steroid and peptides production by the gonads.

In addition, anosmia (loss of the sense of smell) occurs in instances of IHH that are the result of Kallmann syndrome, which is responsible for approximately 50% of all cases of the condition. Other causes of IHH include GnRH insensitivity, which is the second most common cause of IHH and is thought to be responsible for up to 20% of cases, and a minority (less than 5-10%) due to inactivating mutations in a variety of other genes which positively regulate GnRH secretion.

**Secondary HH**, also known as acquired or syndromic HH, is far more common than primary HH, and is responsible for most cases of the condition. It has a multitude of different causes, including brain or pituitary tumors, pituitary apoplexy (bleeding into or impaired blood supply of the pituitary gland), head trauma, ingestion of certain drugs, and certain systemic diseases and syndromes.
Primary and secondary HH can also be attributed to a genetic trait inherited from the biologic parents. Hormone replacement can be used to initiate puberty and continue if the gene mutation occurs in the gene coding for the hormone.

2. **Hypergonadotropic hypogonadism (HH)**

Also known as primary or peripheral/gonadal hypogonadism, is a condition which is characterized by hypogonadism due to an impaired response of the gonads to the gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), and in turn a lack of sex steroid production and elevated gonadotropin levels (as an attempt of compensation by the body). HH may present as either congenital or acquired, but the majority of cases are of the former nature.

There are a multitude of different etiologies of HH. Congenital causes include the following:

- Chromosomal abnormalities (resulting in gonadal dysgenesis) - Klinefelter's syndrome, Turner syndrome, and 45 X/46 XY mosaicism.
- Defects in the enzymes involved in the gonadal biosynthesis of the sex hormones.
- Gonadotropin resistance (e.g., due to inactivating mutations in the gonadotropin receptors).

Acquired causes (due to damage to or dysfunction of the gonads) include gonadal torsion, vanishing/anorchia, orchitis, trauma, surgery, autoimmunity, chemotherapy, radiation, infections (e.g., sexually-transmitted diseases), toxins (e.g., endocrine disruptors), and drugs (e.g., antiandrogens, opioids, alcohol).

**Associated disease**

- gonadal torsion
- anorexia nervosa
- vanishing/anorchia
- autoimmune diseases
- Klinefelter syndrome
- Turner syndrome
- 45x/46xy mosaicism
- brain, pituitary tumors
- pituitary apoplexy
- systemic diseases and syndromes
- 17-α hydroxylase deficiency (a rare genetic disorder of steroid synthesis)
- 17,20 lyase deficiency (a condition that affects the function of the gonads)
- 17-β hydroxysteroid dehydrogenase 3 deficiency (a condition that affects male sexual development)
- lipid congenital adrenal hypoplasia (a rare disorder of steroid synthesis)
- Leydig cell hypoplasia (a condition that affects male sexual development which is characterized by underdevelopment of Leydig cells in the testes)

**Risk factors**

- chronic alcoholism
- medications (e.g., opioids, anabolic steroids, and glucocorticosteroid, opioid analgesics, antidepressants cimetidine, spironolactone, and antifungal drugs)
- head or testicular trauma
- head or testicular surgery
- orchitis
- radiation
- infection
- toxins

**Impact on fertility**

When plasma testosterone levels are below a minimum level, many aging men experience symptoms of low libido, changes in erectile function, and possibly changes in morning erection frequency.

Low testosterone levels can lead to reduced sperm production (oligospermia) sometimes even azoospermie (absence of sperms in ejaculate), which leads to lower possibility of natural conception, due to less sperms capable of reaching the egg.
Female menstruation and ovulation is triggered by hormones such as estrogens, lutenizing hormone, progesterones and follicle stimulating hormone. All of them are controlled by gonadotropins. If the levels of gonadotropins drop, the menstruation and ovulation will not occur. All these processes are neccessary for natural conceptions, because without egg produced during ovulation, it is not possible to conceive a child.

**Prevention**

Hypogonadism cannot be prevented, but it is possible to reduce risk factors by avoiding alcohol, avoiding drugs and maintaining healthy lifestyle.

**Symptoms**

- impaired muscle
- increased body fat
- decreased energy
- increased sleepiness
- sleep disturbance
- poor concentration and memory
- visceral obesity (body fat that's stored within the abdominal cavity around a number of important internal organs such as the liver, pancreas and intestines)
- osteopenia
- depression
- beard development
- reduced height
- reduced body hair
- enlarged breasts
- sexual difficulties
- late, incomplete or lack of development at puberty
- sometimes short stature or the inability to smell
- penis and testes enlargement
- deepening voice
- low libido
- infertility
- oligospermia
- azoospermia
- lack of menstruation
- anovulation
- slow or absent breast growth
- hot flashes
- milky discharge from your breasts

**Therapies**

**Self therapy**

Get a good night's sleep, because lack of sleep can greatly reduce a healthy young man's testosterone levels.

Overweight men with prediabetes are also likely to have lower testosterone. Men with a normal weight have a lower risk of developing diabetes as well as hypogonadism.

No self therapy is known for women.

**Conventional medicine**

Hypogonadism is a condition, which can be treated with hormonal replacement therapy, but it will not
suit for every case.

Surgical therapy is the option for brain tumors.

**Pharmacotherapy**

There must be a definitive diagnosis of hypogonadism before the treatment is initiated. Borderline testosterone levels alone are not necessarily an indication to begin testosterone replacement therapy. If testosterone level drops under borderline level, it must be replaced with hormonal replacement therapy.

The goal of testosterone therapy is to raise serum testosterone level into the midnormal range (400–700 ng/dL) and resolution or reduction in symptoms of hypogonadism. However, the ultimate goals of therapy are to reduce disease and disability, maintain or improve quality of life, and hopefully add vitality to the years.

There are several types of testosterone preparations that are available including testosterone injections, scrotal and nonscrotal transdermal patches, oral testosterone, buccal testosterone, and testosterone gel preparations. Medications that stimulate the production of endogenous testosterone (i.e., hCG, clomiphene) may be used in the treatment of older men when fertility is an issue.

Aging males who are started on testosterone replacement therapy should be followed periodically. After the initiation of testosterone replacement therapy, subjects should have a clinic visit, within 3 months, to make needed dosage and formulation adjustments. Subjects should have regular visits (3 to 6 months after treatment initiation and then annually) for assessment of symptom improvement.

Hormonal replacement pills or skin patch are the option for girls and women suffering from hypogonadism. This hormonal replacement can be sufficient to induce ovulation again. Some of these female can have a low sex drive, which can be managed with low-dose of testosterone.

**Surgical therapy**

Surgical therapy can be an option in cases of brain tumor.

**Assisted reproduction**

If conservative medical treatments fail to achieve a full term pregnancy, the physician may suggest the patient the methods of assisted reproduction techniques (ART).

Assisted reproduction techniques generally start with stimulating the ovaries to increase egg production. Most fertility medications are agents that stimulate the development of follicles in the ovary. Examples are gonadotropins and gonadotropin releasing hormone.

After stimulation, the physician surgically extracts one or more eggs from the ovary, and unites them with sperm in a laboratory setting, with the intent of producing one or more embryos. Hypogonadotropic hypogonadism is characterized by oligospermia or azoospermia and low testosterone. Microscopic epididymal sperm aspiration (MESA) or testicular sperm extraction (TESE) is the method of choice for recovering sperms for in vitro fertilization (IVF).

Fertilization takes place outside the body, and the fertilized egg is reinserted into the woman’s reproductive tract, in a procedure called embryo transfer.

**Find more about related issues**

Diagnoses
Varicocele
An abnormal enlargement of the pampiniform venous plexus in the scrotum.
Learn more at: www.fertilitypedia.org/therapy/diag/varicocele

Azoospermia
Complete absence of sperm in the ejaculate of a man.
Learn more at: www.fertilitypedia.org/therapy/diag/azoospermia

Erectile dysfunction
The inability (that lasts more than 6 months) to develop or maintain an erection of the penis during sexual activity.
Learn more at: www.fertilitypedia.org/therapy/diag/erectile-dysfunction

Obesity
A disease of excess body fat that can have a negative effect on health, leading to reduced life expectancy and other health problems.
Learn more at: www.fertilitypedia.org/therapy/diag/obesity

Polycystic ovary syndrome
A condition in which a woman has an imbalance of female sex hormones. This may lead to changes in the menstrual cycle, cysts in the ovaries, trouble g
Learn more at: www.fertilitypedia.org/therapy/diag/polycystic-ovary-syndrome

Anovulation
Failure of the ovaries to release an oocyte over a period of time generally exceeding 3 months.
Learn more at: www.fertilitypedia.org/therapy/diag/anovulation

Undescended testes
In the case of cryptorchidism one or both testes are absent from the scrotum. It is is the most common etiologic factor of azoospermy in the adult.
Learn more at: www.fertilitypedia.org/therapy/diag/undescended-testes

Ejaculatory disorders
A class of sexual disorders defined as the subjective lack of normal ejaculation.
Learn more at: www.fertilitypedia.org/therapy/diag/ejaculatory-disorders

Turner syndrome
Turner syndrome is a genetic disorder in which a female is partly or completely missing one X chromosome that results in ovarian dysgenesis.
Learn more at: www.fertilitypedia.org/therapy/diag/turner-syndrome

Klinefelter syndrome
The set of symptoms that result from two or more X chromosome in males.
Learn more at: www.fertilitypedia.org/therapy/diag/klinefelter-syndrome

Kallmann syndrome
A genetic condition where the primary symptom is a failure to start puberty or a failure to fully complete puberty.
Learn more at: www.fertilitypedia.org/therapy/diag/kallmann-syndrome

Non-obstructive azoospermia
Complete absence of sperm in the ejaculate due to testicular failure.
Learn more at: www.fertilitypedia.org/therapy/diag/non-obstructive-azoospermia

XX male syndrome
The male sex chromosomal disorder characterized by a spectrum of clinical presentations, ranging from ambiguous to normal male genitalia.
Learn more at: www.fertilitypedia.org/therapy/diag/xx-male-syndrome
Delayed ejaculation
A man’s inability for or persistent difficulty in achieving orgasm, despite typical sexual desire and sexual stimulation.
Learn more at: www.fertilypedia.org/therapy/diag/delayed-ejaculation

Amenorrhoea
The absence of a menstrual period in women of reproductive age.
Learn more at: www.fertilypedia.org/therapy/diag/amenorrhoea

Hyperprolactinemia
The presence of abnormally high levels of prolactin in the blood.
Learn more at: www.fertilypedia.org/therapy/diag/hyperprolactinemia

Noonan syndrome
A frequent autosomal dominant developmental disorder primarily characterized by short stature, typical facial features and heart defects.
Learn more at: www.fertilypedia.org/therapy/diag/noonan-syndrome

Hypoestrogenism
A lower than normal level of estrogen which is the primary sex hormone in women.
Learn more at: www.fertilypedia.org/therapy/diag/hypoestrogenism

Hypoandrogenism
A medical condition characterized by not enough androgenic activity in the body.
Learn more at: www.fertilypedia.org/therapy/diag/hypoandrogenism

Organs

Fallopian tubes
Two very fine tubes that transport sperm toward the egg, and allow passage of the fertilized egg back to the uterus for implantation.
Learn more at: www.fertilypedia.org/edu/organs/fallopian-tubes

Hypothalamus
A region of the forebrain that regulates body temperature, some metabolic processes and governs the autonomic nervous system.
Learn more at: www.fertilypedia.org/edu/organs/hypothalamus

Ovary
The ovum-producing organs of the internal female reproductive system
Learn more at: www.fertilypedia.org/edu/organs/ovary

Penis
External male sex organ that additionally serves as the urinal duct.
Learn more at: www.fertilypedia.org/edu/organs/penis

Pituitary gland
An endocrine gland, about the size of a pea, whose secretions control the other endocrine glands and influence growth, metabolism, and maturation.
Learn more at: www.fertilypedia.org/edu/organs/pituitary-gland

Testes
Male gonads which produce both sperm and androgens, such as testosterone, and are active throughout the reproductive lifespan of the male.
Learn more at: www.fertilypedia.org/edu/organs/testes
Reproductive cells

Oocyte
A female germ cell involved in reproduction.
Learn more at: www.fertilitypedia.org/edu/reproductive-cells/oocyte

Sperm
A male reproductive cell which is able to fertilize the counterpart female gamete - the oocyte.
Learn more at: www.fertilitypedia.org/edu/reproductive-cells/sperm

Spermatogonium
An undifferentiated male germ cell with self-renewing capacity representing the first stage of spermatogenesis.
Learn more at: www.fertilitypedia.org/edu/reproductive-cells/spermatogonium

Biological control

Estradiol
A steroid and estrogen sex hormone produced in the ovaries of females.
Learn more at: www.fertilitypedia.org/edu/biological-control/estradiol

Estrogen
The primary female sex hormone responsible for the development and regulation of the female reproductive system and secondary sex characteristics.
Learn more at: www.fertilitypedia.org/edu/biological-control/estrogen

Follicle-stimulating hormone
FSH is a hormone secreted by the anterior pituitary gland. It regulates the development, growth, pubertal matur and reproductive functions of the body.
Learn more at: www.fertilitypedia.org/edu/biological-control/follicle-stimulating-hormone

Gonadotropin-releasing hormone
A releasing hormone responsible for the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary.
Learn more at: www.fertilitypedia.org/edu/biological-control/gonadotropin-releasing-hormone

Luteinizing hormone
A hormone, that stimulates ovulation and the development of the corpus luteum in females, and the production of androgens in males.
Learn more at: www.fertilitypedia.org/edu/biological-control/luteinizing-hormone

Progesterone
Steroid hormone, secreted by the ovaries, whose function is to prepare the uterus for the implantation of a fertilized ovum and to maintain pregnancy.
Learn more at: www.fertilitypedia.org/edu/biological-control/progesterone

Testosterone
Steroid hormone produced primarily in the testes of the male; responsible for the development of secondary sex characteristics in the male.
Learn more at: www.fertilitypedia.org/edu/biological-control/testosterone

Reproductive functions
Erection
The physiological process by which a penis becomes erect by being engorged with blood.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/erection

Fertilization
The fusion of an ovum with a sperm to initiate the development of a new individual organism.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/fertilization

Oogenesis
The process of the maturation of the female gametes through the meiotic division.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/oogenesis

Ovulation
The release of egg(s) from the ovaries.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/ovulation

Spermatogenesis
Process in which spermatozoa are produced from male primordial germ cells in testicles by way of mitosis and meiosis.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/spermatogenesis

⚠️ Risk factors

Hemochromatosis
An accumulation of iron in the body from any cause.
Learn more at: www.fertilitypedia.org/therapy/rf/hemochromatosis

High level of FSH
FSH levels above what an expected levels for one’s age and is indicator of proper ovarian function.
Learn more at: www.fertilitypedia.org/therapy/rf/high-level-of-fsh

High level of LH
A condition with high blood luteinizing hormone (LH) leading to irregular periods and reduced fertility in both females and males.
Learn more at: www.fertilitypedia.org/therapy/rf/high-level-of-lh

Low level of estrogen
A diminished level of blood estrogen level.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-estrogen

Low level of FSH
A condition with low serum follicle-stimulating hormone (FSH) concentration.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-fsh

Low level of LH
A serum luteinizing hormone (LH) levels under normal serum concentration for gender and age.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-lh

Low level of testosterone
An abnormally low testosterone production which may occur because of testicular or hypothalamic-pituitary dysfunction.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-testosterone

Mumps
An infection that primarily affects the parotid glands, caused by the mumps virus which can impair male fertility.
Learn more at: www.fertilitypedia.org/therapy/rf/mumps
**Symptoms**

**Absence of menstrual periods**
The absence of a menstrual period in a woman of reproductive age.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/absence-of-menstrual-periods](www.fertilitypedia.org/edu/symptoms/absence-of-menstrual-periods)

**Delayed puberty**
An organism has passed the usual age of onset of puberty with no physical or hormonal signs.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/delayed-puberty](www.fertilitypedia.org/edu/symptoms/delayed-puberty)

**Disturbed sense of smell**
A qualitative and quantitative alteration or distortion of the perception of smell.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/disturbed-sense-of-smell](www.fertilitypedia.org/edu/symptoms/disturbed-sense-of-smell)

**Enlarged breasts in men**
Enlargement and swelling of breast tissue in men.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/enlarged-breasts-in-men](www.fertilitypedia.org/edu/symptoms/enlarged-breasts-in-men)

**Gynecomastia**
A disorder of the endocrine system in which there is a non-cancerous swelling of the breast tissue in boys or men.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/gynecomastia](www.fertilitypedia.org/edu/symptoms/gynecomastia)

**Hypospadias**
A birth defect of the urethra in the male where the urinary opening is not at the usual location on the head of the penis.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/hypospadias](www.fertilitypedia.org/edu/symptoms/hypospadias)

**Impaired muscle and beard development**
Reduced body hair and loss of muscle mass in males.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/impaired-muscle-and-beard-development](www.fertilitypedia.org/edu/symptoms/impaired-muscle-and-beard-development)

**Infertility**
The failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/infertility](www.fertilitypedia.org/edu/symptoms/infertility)

**Lack of breasts development and menstrual periods**

**Low facial and body hair growth**
Decrease of facial and body hair in males.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/low-facial-and-body-hair-growth](www.fertilitypedia.org/edu/symptoms/low-facial-and-body-hair-growth)

**Lowered libido**
The absence of sexual appetite.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/lowered-libido](www.fertilitypedia.org/edu/symptoms/lowered-libido)

**Reduced height**
A height of a human being which is below typical.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/reduced-height](www.fertilitypedia.org/edu/symptoms/reduced-height)

**Small penis**
An adult penis with an erect length of less than 7 cm or 2.76 inches.  
Learn more at: [www.fertilitypedia.org/edu/symptoms/small-penis](www.fertilitypedia.org/edu/symptoms/small-penis)
Small testes
Abnormally small testicular volume.
Learn more at: www.fertilitypedia.org/edu/symptoms/small-testes

Therapies

Egg donation
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: www.fertilitypedia.org/edu/therapies/egg-donation

Embryo donation
The giving of embryo to another person or couple for conception or to research.
Learn more at: www.fertilitypedia.org/edu/therapies/embryo-donation

ICSI
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: www.fertilitypedia.org/edu/therapies/icsi

Laser-assisted immotile sperm selection
Method, which uses a laser to identify viable sperm cell, recommended in MESA/TESA IVF cycles or in patients diagnosed with sperm immotility.
Learn more at: www.fertilitypedia.org/edu/therapies/laser-assisted-immotile-sperm-selection-1

Micro TESE
Microsurgical method used to identify areas of sperm production within the testes with the aid of optical magnification.
Learn more at: www.fertilitypedia.org/edu/therapies/micro-tese

PESA
Sperm aspiration procedure in which a needle is inserted into the epididymis in order to retrieve sperm.
Learn more at: www.fertilitypedia.org/edu/therapies/pesa

Preimplantation genetic diagnosis
Technology that allows couples with a family history of monogenic disorders, x-linked diseases and chromosomal abnormality have a healthy baby.
Learn more at: www.fertilitypedia.org/edu/therapies/preimplantation-genetic-diagnosis

Preimplantation genetic screening
The term PGS is used to denote procedures that do not look for a specific disease but to identify embryos at risk of de-novo occurring aneuploidies
Learn more at: www.fertilitypedia.org/edu/therapies/preimplantation-genetic-screening-1

Sperm donation
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: www.fertilitypedia.org/edu/therapies/sperm-donation

Standard IVF
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: www.fertilitypedia.org/edu/therapies/standard-ivf

TESE
Removal of a small portion of testicular tissue in order to extract a few viable sperm.
Learn more at: www.fertilitypedia.org/edu/therapies/tese

Sources
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