HYPERGONADOTROPIC HYPOGONADISM
Primary Hypogonadism, Peripheral Hypogonadism, Gonadal Hypogonadism, Hh

Decreased functional activity of the gonads, with retardation sexual development, associated with high levels of hormones that stimulate the gonads.

Related Diagnoses:
Undescended testes | Non-obstructive azoospermia

About Hypergonadotrophic hypogonadism

Hypergonadotrophic hypogonadism (HH) is a condition with decreased functional activity of the gonads, with retardation sexual development, which is associated with secretion of high levels of gonadotropins.

Hyponadism means diminished functional activity of the gonads—the testes in males or the ovaries in females—that may result in diminished sex hormone biosynthesis (the formation of chemical compounds by a living organism). Sex hormones are necessary for control of secondary sex characteristics such as testicular development in men and breast development in women. For both sexes pubic hair growth is common sex characteristic. Menstrual cycle and sperm production is also controlled by sex hormones.

Physicians measure gonadotropins (luteinizing hormone- LH and follicle stimulating hormone- FSH) to distinguish hypergonadotrophic from hyponadotrophic hypogonadism. In hypergonadotrophic (also known as primary) hypogonadism the LH and/or FSH are usually elevated, meaning the problem is in the testicles or ovaries, whereas in hyponadotrophic (also known as secondary) hypogonadism, both are normal or low, suggesting the problem is in the brain.

Hypergonadotrophic hypogonadism may present as either congenital or acquired, but the majority of cases are of the former nature.

Congenital causes include the following:

- Chromosomal abnormalities - Turner’s syndrome (a condition in which a female is partly or completely missing an X chromosome, Pic. 1), Klinefelter’s syndrome (the set of symptoms that result from two or more X chromosomes in males, Pic. 2), Swyer’s syndrome (a rare disorder characterized by the failure of the male sex glands to develop), and XX gonadal dysgenesis (a type of hypogonadism in a person whose karyotype is 46,XY).
- 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) - Leydig cell hypoplasia (or insensitivity to LH) in males, FSH insensitivity in females.

Acquired causes (due to damage to or dysfunction of the gonads) include ovarian torsion, vanishing/anorchia (the absence of both testes at birth), orchitis (an inflammation of testicles), premature ovarian failure (a loss of normal function of your ovaries before age 40), ovarian resistance syndrome (a cause of ovarian failure that can lead to absence of menstrual cycles), trauma, surgery, autoimmunity, chemotherapy, radiation, infections (e.g., sexually transmitted diseases), toxins (e.g., endocrine disruptors), and drugs (e.g., antiandrogens, opioids, alcohol).
If there is suspicion that patients suffer from hypogonadism, the first round of testing will involve checking sex hormone levels. A blood sample will be checked for FSH and LH levels. Testosterone and estrogen are other hormones which have to be measured. Sometimes these hormones are decreased because of anemia which can be caused by iron deficiency.

To exclude secondary hypogonadism, hormones and function of pituitary gland must be checked.

HH can be treated with hormonal replacement therapy.

Associated diseases

- Klinefelter syndrome
- Turner syndrome
- mumps
- varicocele (an abnormal enlargement of the venous plexus in the scrotum)
- Swyer’s syndrome
- XX gonadal dysgenesis

Complications

The hypergonadotropic hypogonadism with very early onset which persists into adulthood is associated not only with a decreased pubertal peak bone mass but also with a high bone turnover state and an increased risk of falling (due to the decreased muscle strength and possible associated vitamin D deficiency), all leading to fragility fractures.

In adult men low testosterone levels are an independent risk factor for hip fracture especially in the elderly, and the replacement therapy has a beneficial effect, increasing the lumbar and hip bone mineral density (BMD).

Risk factors

- ovarian torsion
- vanishing/anorchia
- orchitis
- premature ovarian failure (POF)
- ovarian resistance syndrome
- trauma
- surgery
- autoimmunity
- chemotherapy
- radiation
- infections
- toxins
- drugs

Impact on fertility

Congenital HH is associated with failure of sperm development and the process of ovulation. With lack of hormones, these processes will not happened and without sperm and egg, the pregnancy is not possible.

In case of acquired HH, the most frequent cause in women is premature ovarian failure. Women suffering from premature ovarian failure (POF) experience similar symptoms to natural menopause; however, these symptoms are also accompanied by an earlier loss of fertility. Therefore, women at risk of POF who delay childbearing until after their 30s may experience problems conceiving and carrying a pregnancy to full term. This loss of fertility can be due to an accelerated loss of follicles, an inability of the remaining follicles to respond to ovulatory signals, an initially reduced ovarian reserve (a term that is used to determine the capacity of the ovary to provide egg cells that are capable of fertilization resulting in a healthy and successful pregnancy) at the time of birth, or a combination of all.

Processes which can cause male acquired HH such as orchitis, trauma, radiation and ect., often lead to azoospermia. Azoospermia is defined as the complete absence of spermatozoa upon examination of the semen (including capillary tube centrifugation, strictly confirmed by the absence of spermatozoa issued in urine after ejaculation). It can be divided into non obstructive azoospermia (no sperm in the semen because of abnormal
sperm production) or obstructive azoospermia (no sperm in a man’s semen, as a result from problems with sperm delivery).

Hormonal imbalance or lack of hormonal stimulation is the main reason of non obstructive azoospermia. If we manage to improve this imbalance, there is possibility to conceive child the natural way. In other cases, we have to use techniques of assisted reproduction.

In obstructive azoospermia sperm are produced but not ejaculated. In these cases we need to fix the obstruction, or get the sperm itself.

**Prevention**

This condition cannot be prevented.

**Symptoms**

*Both sexes*

Examples of symptoms of hypergonadotrophic hypogonadism in both sexes include delayed, reduced, or absent puberty, low libido, and infertility.

*Female symptoms*

Women with hypergonadotrophic hypogonadism do not begin menstruating and it may affect their height and breast development. Onset in women after puberty causes cessation of menstruation, loss of body hair and hot flashes.

*Male symptoms*

Hypergonadotrophic hypogonadism in men is a syndrome characterized by low serum testosterone levels. These symptoms include erectile dysfunction, decreased vitality, decreased muscle mass, increased adiposity, depressed mood, osteopenia (a condition in which bone mineral density is lower than normal), and osteoporosis.

**Therapies**

**Self therapy**

No self or alternative therapy can be used to treat hypergonadotrophic hypogonadism.

**Conventional medicine**

Treatment of HH is usually with hormone replacement therapy, consisting of androgen and estrogen administration in males and females, respectively.

This condition does not require surgical therapy.

**Pharmacotherapy**

Male primary or hypergonadogropic hypogonadism is often treated with testosterone replacement therapy. Commonly used testosterone replacement therapies include transdermal (through the skin) using a patch or gel, injections, or pellets. Oral testosterone is no longer used (in the U.S.) because it is
broken down in the liver and rendered inactive; it also can cause severe liver damage.

Like many hormonal therapies, changes take place over time. It may take as long as 2–3 months at optimum level to reduce the symptoms, particularly the wordfinding and cognitive dysfunction.

Testosterone levels in the blood should be evaluated to ensure the increase is adequate.

For women with hypogonadism, estradiol and progesterone are often replaced. Some physicians also give testosterone to women, mainly to increase libido.

**Surgical therapy**

There is no surgical therapy of this condition.

**Assisted reproduction**

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

Assisted reproductive technology (ART) is the technology used to achieve pregnancy in procedures such as fertility medication, artificial insemination, in vitro fertilization and surrogacy. It is reproductive technology used primarily for infertility treatments, and is also known as fertility treatment. It mainly belongs to the field of reproductive endocrinology and infertility, and may also include intracytoplasmic sperm injection (ICSI) and cryopreservation. Some forms of ART are also used with regard to fertile couples for genetic reasons (preimplantation genetic diagnosis). ART is also used for couples who are discordant for certain communicable diseases; for example, HIV to reduce the risk of infection when a pregnancy is desired.

In case of premature ovarian failure with no eggs left or inability of the remaining follicles to respond to ovulatory signals, egg donation is option for pregnancy. Egg donation is the process by which a woman donates eggs for purposes of assisted reproduction. Egg donation typically involves in vitro fertilization (IVF) technology, with the eggs being fertilized in the laboratory. The fertilized eggs (embryos) are cultivated under very stringent conditions and examined every day by the embryologist to evaluate their progress. The embryos are usually cultured for 3 to 5 days, before the best one(s) are selected to be put (transferred) in to the womb.

Intracytoplasmic sperm injection (ICSI) is beneficial in the case of male factor infertility where sperm counts are very low or failed fertilization occurred with previous IVF attempt(s). The ICSI procedure involves a single sperm carefully injected into the center of an egg using a microneedle. With ICSI, only one sperm per egg is needed. Without ICSI, you need between 50,000 and 100,000.

Two techniques that enable to some extent the selection of physiologically normal spermatozoa have recently been developed. One of these is termed intracytoplasmic morphology-selected sperm injection (IMSI). Here, spermatozoa are selected for ICSI and analysed digitally prior to the microinjection procedure in order to deselect morphologically abnormal spermatozoa. With this technique, abnormalities not visible in standard ICSI procedures have been observed. IMSI increases the pregnancy rate during ICSI cycles, and some data suggests that the level of pregnancy termination is also decreased. A second technique recently introduced to assisted reproduction is that of sperm selection with hyaluronic acid (HA), e.g. PICSI. In this technique, mature sperm with HA receptors are distinguished from immature and abnormal sperm since these do not express such receptors.

In patients with obstructive azoospermia, if reconstructive surgery fails or is not feasible, microscopic epididymal sperm aspiration (MESA) or testicular sperm extraction (TESE) is the method of choice for recovering spermatozoa. In patients with non-obstructive azoospermia, TESE is usually used for obtaining several spermatozoa as a male therapeutic approach in IVF. In the case of genetic-related azoospermia, PGD/PGS of early embryos is strongly recommended.

The rate of success for IVF is correlated with a woman’s age. More than 40 percent of women under 35 succeed in giving birth following IVF, but the rate drops to a little over 10 percent in women over 40.
Find more about related issues

**Diagnoses**

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

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

**Symptoms**

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

**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

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

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

**Gallery**
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