TESTICULAR FAILURE

Primary Hypogonadism

The inability of the testicles to produce sperm or testosterone.

診断

Related Diagnoses:
- Azoospermia
- Non-obstructive azoospermia
- XX male syndrome
- Hyperprolactinemia
- Gonadal dysgenesis

About Testicular failure

Testicular failure (TF) is referring to the condition of testicles which are unable to produce sperm or testosterone. Testosterone is the essential androgen (male sex hormone) for male reproductive function that allows for the development of male genitalia, secondary sex characteristics in prepubescent males, and the maintenance of secondary sex characteristics, initiation and maintenance of spermatogenesis (the sperm cell development), and stimulation and maintenance of sexual function in postpubescent males. Therefore, its low production causes decreased sperm production and change of the body aspect among other effects. Androgen deficiency in young pre-pubertal boys causes delayed puberty, decreased muscle mass and hair growth and prohibits the development of typical male deep voice etc. Testicular failure may manifest by reduced libido, sexual dysfunction (erectile dysfunction) in adolescent men. Any man with testosterone deficiency is in increased risk of osteoporosis.

There are several known causes of testicular failure:

Klinefelter’s syndrome
As a typical inherited condition connected with testicular failure, Klinefelter’s syndrome should be mentioned. It is the condition resulting from a congenital abnormality of 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 testes and testicular torsion**

Cryptorchidism is another condition with possible congenital origin. It is referring to the state when one or both testicles don’t move down to the scrotum. If the condition is not corrected in early childhood, it may lead to malfunction of the testicles and reduced production of testosterone. Testicular torsion occurs when the spermatic cord (from which the testicle is suspended) twists, cutting off the testicle's blood supply, a condition called ischemia. The principal symptom is rapid onset of testicular pain. As the consequence of abrupt blood supply, testosterone cannot be flushed out.

**Testicular infections**

Primary testicular failure may also appear due to infections. Mumps and orchitis may cause long-term testicular damage and consequential malfunction of testicles (resulting in lowered 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.

**Others causes**

Injuries of testicles are not uncommon as the testicles are located outside the abdomen. The damage done to testicles may cause primary hypogonadism. If only one testicle is damaged, it may cause decreased testosterone production.

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.
The proper function of testicles may be also corrupted by elevated iron levels circulating in blood.

The diagnosis of TF is made upon observation of clinical manifestations mentioned above in combination with analysis of testosterone levels circulating within the blood. 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.

Hormonal replacement therapy (artificial testosterone supplementation) is the most common step while attending this condition. Depending on the cause, the therapy may include some other approaches. In case of inflammatory diseases, the treatment consists in curing the infection responsible for decreased testicular function. The proper function of testicles in such cases is usually restored. The malformations of reproductive apparatus may be often solved by surgical intervention. If the TF is caused by an inherited condition, it cannot be healed so the therapy focuses on managing the symptoms related with testosterone deficiency.

Associated diseases

- Klinefelter syndrome
- Noonan syndrome (congenital disorder associated with cryptorchidism)
- Leydig cell hypoplasia (Leydig cells do not develop)
- Mumps
- Sertoli cell only syndrome (SCOS)
- varicocele (venous malformation within the testes)
- azoospermia (reduced sperm production)
- gonadal dysgenesis (genetically predisposed condition inducing the malformation of reproductive organs)
- orchitis (testicular inflammation)
- cryptorchidism (undescended testicles)

Complications

- infertility
- increased risk of prostate cancer
- delayed puberty

Risk factors

- infections of reproductive apparatus
- genetic predispositions
Impact on fertility

The low levels of testosterone lead to reduced fertility. Androgen deficiency affects testicular sperm nursing cell (Sertoli cells) which are responsible for conducting the sperm development. Insufficient stimulation of Sertoli cells by testosterone may manifest by decreased sperm production or by arrest of spermatogenesis. Klinefelter’s syndrome is associated with complete infertility.

Androgen deficiency may also cause sexual dysfunction in men. As testosterone affects the sexual desire, its low concentrations may be responsible for reduced libido. Erectile dysfunction is a common symptom related to reduced libido and male sex hormones imbalance.

In case of non-hormonal causes, such as missing germ cells within the seminiferous tubules (SCOS), there is no fertility potential in affected person. The germ cells represent the first stage of sperm cell development; without them the spermatogenesis cannot proceed.

In case of physical trauma/inflammation in the testicular area, the common reaction is a local inflammation of the tissues. This increases the blood flow and temperature within the testicles. There is also higher concentration of so called reactive oxygen species (ROS). As successful spermatogenesis requires quite specific temperature, even small changes may induce sperm damage. ROS has also negative impact on sperm cell quality negatively influencing its membrane and genetic information held within. The impact of physical trauma on testicular function depend on its severity.

Prevention

In case of congenitally transmitted condition, such as Klinefelter’s syndrome, there is no way to prevent the testicular failure.

Regarding testicular damage, the avoidance of risky activities is
recommendable. It is also known that constant low level damage, which may be induced for example by bicycling, may induce testicular failure.

As the testicular failure may be caused by infections of reproductive apparatus, it is also recommendable to maintain high hygiene standards.

**Symptoms**

Signs absence or regression of secondary sex characteristics (e.g. gynecomastia, the development of “male breasts”), anaemia, muscle wasting, reduced bone mass or bone mineral density, oligospermia (reduced sperm count), 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, anaemia, osteoporosis, and hot flushes. In the pre-pubertal male, if treatment is not initiated, signs and symptoms include sparse body hair.

**Therapies**

**Self therapy**

None.

**Conventional medicine**

**Pharmacotherapy**

**Hormonal replacement therapy (HRT)**

Hormonal replacement therapy (HRT) is the basic approach to treat testicular failure. The goals of HRT depend on the cause of testicular failure. Generally, the restoration of sexual function, libido enhancement, mood stabilization, prevention of osteoporosis are the main targets. In case of some forms of testicular failure such as Klinefelter's syndrome, the restoration of normal testicular function cannot be achieved yet it is beneficial as a prevention for development.
There are several ways to supplement testosterone to a patient including transdermal patches, topical gels, buccal tablets, implantable pellet, intramuscular injections and oral tablets. Each way has its own risks and benefits.

**Surgery**

There is no surgical treatment available to solve this particular disorder.

**Assisted reproduction**

Assisted reproduction offers various ways to solve fertility issues connected with testicular failure. The choose of each specific method depends on the severity of the disorder.

The surgical retrieval of living sperm may be done if there is at least partial sperm production maintained in the testicles. In such cases the techniques like microsurgical epididymal sperm aspiration (MESA), percutaneous epididymal sperm aspiration (PESA) can be used to obtained from epididymis. If there cannot be found living sperm cell, there is still a way to retrieve living sperm cell directly from testicles by using the testicular sperm extraction (TESE) which is used to remove small part of testicular tissue containing sperm cells. Testicular sperm aspiration (TESA) is kind of a similar technique which extracts just fluids containing living sperm cells from the testicle.

If those methods would fail or the patient suffering from testicular failure is unable to produce any sperm at all, the use of donated sperm cells is recommendable. The donor of sperm must undergo series of tests and examination to ensure the healthiness of retrieved sample which is stored afterwards within liquid nitrogen (cryopreservation). Thanks to great advance of cryopreservation technique, the fertilization capacity and quality of stored sperm is maintained at high level and now days there is a quite large list of donor from which the patient may choose.

Retrieved or donated sperm cells are consequentially used to fertilize the oocyte under laboratory conditions. Depending on the count of usable living sperm cells two techniques are routinely performed. With sufficient count of living sperm cells (up to hundreds) standard in vitro
fertilization (IVF) can be performed. The retrieved sperm cells are placed in a special dish containing a healthy oocyte and a special medium simulating natural conditions so the fertilization may occur. If there is only few sperm cells available after the retrieval, the intra cytoplasmic sperm injection (ICSI) is used. This technique uses just single sperm cell which is directly inserted by microneedle into the oocyte and the fertilization takes place.

Find more about related issues

Diagnoses

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

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

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

Gonadal dysgenesis
Any congenital developmental disorder of the reproductive system characterized by a progressive loss of germ cells on the developing gonads.
Learn more at: www.fertilitypedia.org/therapy/diag/gonadal-dysgenesis

Risk factors
**High level of FSH**
It is a condition with high serum FSH concentration. Learn more at: [www.fertiltypedia.org/therapy/rf/high-level-of-fsh](http://www.fertiltypedia.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.fertiltypedia.org/therapy/rf/high-level-of-lh](http://www.fertiltypedia.org/therapy/rf/high-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.fertiltypedia.org/therapy/rf/low-level-of-testosterone](http://www.fertiltypedia.org/therapy/rf/low-level-of-testosterone)

**Symptoms**

**Decreased level of testosterone**
Testosterone levels lower than the reference ranges. Learn more at: [www.fertiltypedia.org/edu/symptoms/decreased-testosterone-level](http://www.fertiltypedia.org/edu/symptoms/decreased-testosterone-level)

**Increased level of FSH**
A condition with high serum follicle–stimulating hormone (FSH) concentration. Learn more at: [www.fertiltypedia.org/edu/symptoms/increased-level-of-fsh](http://www.fertiltypedia.org/edu/symptoms/increased-level-of-fsh)

**Therapies**

**Egg donation**
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research. Learn more at: [www.fertiltypedia.org/edu/therapies/egg-donation](http://www.fertiltypedia.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.fertiltypedia.org/edu/therapies/icsi](http://www.fertiltypedia.org/edu/therapies/icsi)

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

Sources

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