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## **SHORT NOTES ON TESTOSTERONE AND MALE INFERTILITY**

### **1. TESTOSTERONE**

**DEFINITION:** Testosterone is a hormone produced by the human body. It's mainly produced in men by the testicles. Testosterone affects a man's appearance and sexual development. It stimulates sperm production as well as a man's sex drive. It also helps build muscle and bone mass.

The production of testosterone starts to increase significantly during puberty, and begins to dip after age 30 or so.

**SECRETION OF TESTOSTERONE:** Testosterone is produced by the gonads (by the Leydig cells in **testes** in men and by the ovaries in women), although small quantities are also produced by the adrenal glands in both sexes. It is an androgen, meaning that it stimulates the development of male characteristics. The hypothalamus and pituitary gland control how much testosterone the testes produce and secrete. Luteinizing hormone (LH) stimulates **testosterone** production. If too much testosterone is produced, the hypothalamus alerts the pituitary gland to make less LH, which tells the testes to decrease testosterone levels.

**HYPER SECRETION OF TESTOSTERONE:** The effect excess testosterone has on the body depends on both age and sex. It is unlikely that adult men will develop a disorder in which they produce too much testosterone and it is often difficult to spot that an adult male has too much testosterone. More obviously, young children with too much testosterone may enter a false growth spurt and show signs of **early puberty** and young girls may experience abnormal changes to their **genitalia**. In both males and females, too much testosterone can lead to **precocious puberty** and result in infertility.

In women, high blood levels of testosterone may also be an indicator of **polycystic ovary syndrome**. Women with this condition may notice increased acne, body and facial hair called **hirsutism**, balding at the front of the hairline, increased muscle bulk and a deepening voice. Various diseases or hormonal disorders can cause hormonal changes in women. The most common causes of high testosterone levels in women are hirsutism, polycystic ovary syndrome, and congenital adrenal hyperplasia.

### **HYPOSECRETION OF TESTOSTERONE:**

If **testosterone** deficiency or hypo secretion of testosterone occurs during fetal development, then male characteristics may not completely develop. If testosterone deficiency occurs during puberty, a boy's growth may slow and no growth spurt will be seen. The child may have reduced development of pubic hair, growth of the penis and testes, and deepening of the voice. Around the time of puberty, boys with too little testosterone may also have less than normal strength and

endurance, and their arms and legs may continue to grow out of proportion with the rest of their body.

In adult men, low testosterone may lead to a reduction in muscle bulk, loss of body hair and a wrinkled 'parchment-like' appearance of the skin. Testosterone levels in men decline naturally as they age. In the media, this is sometimes referred to as the male menopause (andropause).

Low testosterone levels can cause mood disturbances, increased body fat, loss of muscle tone, inadequate erections and poor sexual performance, osteoporosis, difficulty with concentration, memory loss and sleep difficulties. Current research suggests that this effect occurs in only a minority (about 2%) of ageing men.

### **SYNTHESIS OF TESTOSTERONE:**

In the testis, **testosterone biosynthesis** occurs predominantly in Leydig cells located in the interstitial space between the seminiferous tubules. **Testosterone** is **synthesized** starting from cholesterol through a well-characterized steroid biosynthetic pathway involving the sequential action of multiple enzymes

Testosterone biosynthesis by the Leydig cells of the testis proceeds via a sequence of enzymatic steps under the control of LH secretion. There is a negative feedback of testosterone on LH secretion both directly at the pituitary and indirectly at the hypothalamic level. The feedback relationship is developed in early infancy.

### **FUNCTIONS OF TESTOSTERONE**

#### **IN MALES;**

- Responsible for the development of primary sexual development which includes: testicular descent, spermatogenesis, enlargement of the penis and testes.
- Involved in regulating secondary male characteristics, which are those responsible for masculinity which include male hair patterns, vocal changes, and voice deepening, anabolic effects which include growth spurts in puberty and skeletal muscle growth (testosterone stimulates protein synthesis)
- Stimulates erythropoiesis, which results in a higher hematocrit in males versus females.
- Increases sex drive
- body fat distribution
- production of sperm
- mood

#### **IN FEMALES;**

- Testosterone plays a role in the growth and maintenance of female reproductive tissue and bone mass.
- Mood
- It plays a role in women breast health
- fertility

- sex drive
- menstrual health
- vaginal health

### **TRANSPORT OF TESTOSTERONE**

Testosterone is secreted into the blood and carried to target cells in the male reproductive organs. Most of the testosterone is transported bound to a specific plasma protein called sex hormone binding globulin (SHBG). The remainder is termed free testosterone. It is free testosterone that can be converted into DHT but it cannot be converted by aromatase into estradiol. Both DHT and testosterone can bind to the androgen receptor but DHT binds with a greater affinity than unbound or unchanged testosterone. Once bound to the androgen receptor, DHT or testosterone forms a complex that undergoes a structural change. This complex then moves into the nucleus of the cell and binds to specific nucleotide sequences of DNA which are termed hormone response elements.

## **2. MALE INFERTILITY**

**DEFINITION:** Male infertility refers to a male's inability to cause pregnancy in a fertile female. Male infertility is commonly due to deficiencies in the semen, and semen quality is used as a surrogate measure of male fecundity.

### **CAUSES OF MALE INFERTILITY**

**Genetics:** Chromosomal anomalies and genetic mutations account for nearly 10–15% of all male infertility cases e.g. **Klinefelter Syndrome, Y chromosome deletions**

**Y chromosomal infertility** is a direct cause of male infertility due to its effects on sperm production, occurring in 1 out of every 2000 males. Usually affected men show no sign of symptoms other than at times can exhibit smaller testes size. Men with this condition can exhibit azoospermia (no sperm production), oligospermia (small number of sperm production), or they will produce abnormally shaped sperm (teratozoospermia).

- retrograde ejaculation
- varicocele, or the swelling of the veins around the testicles
- testicles that haven't descended into the scrotum
- having antibodies that attack your sperm and destroy them
- a hormonal imbalance, such as low testosterone production
- Age
- Abnormal set of chromosomes
- Neoplasm, e.g. seminoma
- Idiopathic failure
- Cryptorchidism

- Trauma
- Hydrocele
- Hypopituitarism in adults, and hypopituitarism untreated in children (resulting in growth hormone deficiency and proportionate dwarfism.)
- Mumps
- Testicular cancer
- Defects in USP26 in some cases
- Acrosomal defects affecting egg penetration
- Idiopathic oligospermia - unexplained sperm deficiencies account for 30% of male infertility
  
- Various medications and drugs can also affect male fertility, such as: chemotherapy or radiation therapy, which are used for cancer, sulfasalazine which is used for rheumatoid arthritis (RA) or ulcerative colitis (UC), calcium channel blockers, which are used for high blood pressure, tricyclic antidepressants, anabolic steroids, which are used for improved athletic performance or hormonal issues such as delayed puberty, recreational drugs such as marijuana and cocaine

### **SIGNS AND SYMPTOMS OF MALE INFERTILITY**

- Changes in hair growth.
- Changes in sexual desire.
- Pain, lump, or swelling in the testicles.
- Problems with erections and ejaculation.
- Small, firm testicles.
- Recurrent respiratory infections.
- Inability to smell.

### **TREATMENT OF MALE INFERTILITY**

Male infertility can be treated in a variety of ways, depending on the cause. Treatment options for men can include;

- Surgery
- Medication
- Assisted reproductive technology (ART).

Surgery can fix obstructions that are preventing sperm from being present in the ejaculate. It can also correct conditions such as varicocele. In some cases, sperm can be retrieved directly from the testicles after which it can be used in ART treatments.

Medications can be used to treat issues such as hormonal imbalances. They can also be used to treat other conditions that can affect male fertility, such as ED or infections that affect sperm count.

ART refers to treatments in which eggs and sperm are handled outside of the body. It can include treatments such as in vitro fertilization (IVF) and intracytoplasmic sperm injection. Sperm for ART treatments can be received from ejaculate, extraction from the testicles, or a donor.

### **PREVENTION OF MALE INFERTILITY**

- Avoiding smoking because it damages sperm DNA
- Avoiding heavy marijuana and alcohol use.<sup>[39]</sup>
- Avoiding excessive heat to the testes.<sup>[39]</sup>
- Maintaining optimal frequency of coital activity
- Wearing a protective cup and jockstrap to protect the testicles
- Healthy diet