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Testosterone

Kizito Omona

Abstract

Testosterone is a hormone produced majorly by the testicles in adult human men. The hormone affects a man's appearance and sexual development, stimulates sperm production and regulates a man's sex drive. It also helps build muscles and bone mass. Testosterone production decreases with age. Its production is at its highest in a man's early adulthood and drops slowly each year afterwards. The normal range of testosterone in the body is typically 300 to 1000 ng/dL for men and 15 to 70 ng/dL for women. A range of symptoms can occur if its production drastically drops below normal. Men with low T can experience a range of symptoms if its decrease becomes significant. Low testosterone, or low T, is diagnosed when levels fall below 300 ng/dL. A blood test, called 'a serum testosterone test', is used to determine the level of circulating testosterone. When the body does not produce the right amount of testosterone, the condition is called hypogonadism. This is sometimes called "low T". Men diagnosed with hypogonadism can benefit from testosterone therapy. However, therapy is not usually recommended, unless testosterone level falls quite below the normal range for age. This is because there are some natural remedies which can help.

Keywords: low T, Hypogonadism, sex drive, erection, semen volume, mood

1. Introduction

The term Hormones refer to substances or molecules that are produced by the endocrine system. This system sends messages to various parts of the body and hormones are the messengers used to do so. Hormones help to regulate body processes, like hunger, blood pressure and sexual desire, among others. Whereas hormones are key molecules in reproduction in human, they are fundamental to *all* the body systems [1]. Chemically, hormones may be classified as either proteins or steroids. All of the hormones in the human body, except the sex hormones and those from the adrenal cortex, are proteins or protein derivatives [2].

Hormones flow through the whole body by blood but only affect certain cells designed to receive their messages – target cells. These specific cells that respond to a given hormone have receptor sites for the said hormone [1, 2]. This is a sort of lock-and-key mechanism, in that if the hormone fits the receptor site then there will be an effect. It is synonymous with lock and key, where if the key fits, then the lock opens. If a hormone and a receptor do not match, there will be no reaction. In some cases, target cells are localized in a single gland or organ whereas in other instances, they are diffuse and scattered throughout the whole body in which case many areas will be affected. Through modifying activities of the cells, hormones are able to bring about their associated effects on those target cells.

When certain types of hormones called protein hormones react with receptors on the surface of the target cell, the sequence of events that results in hormone

action is relatively fast. On the other hand, steroid hormones basically react with receptor sites inside a target cell. Since this method of action involves synthesis of proteins, the actions of these hormones are relatively slow [2].

2. The male reproductive hormones

2.1 General male reproductive hormones

Male reproductive functions are mediated by different hormones [3]. The 'master' regulator hormonal axis is the hypothalamo-pituitary-gonadal/testicular axis which is led by the pulsatile release of hypothalamic gonadotropin-releasing hormone (GnRH). This, in turn, stimulates anterior pituitary trophic hormones – luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Luteinizing hormone acts upon the testicular cells, the Leydig cells for steroidogenesis while follicle stimulating hormone acts on the Sertoli cells to aid spermatogenesis. This primary axis is influenced by an array of other testicular hormones, metabolic hormones and different regulatory factors. These hormonal cross-talks influence the intricate testicular functions, sexual behavior and semen quality in men, including semen volume [3]. See **Figure 1** for the illustration.

Testes secrete steroids known as androgens. These androgens, in turn, are responsible for maintenance of male characteristics as well as male behaviors. Follicle stimulating hormones (FSH) released from pituitary gland stimulates the growth of the seminiferous tubules. Seminiferous tubules constitute much of the

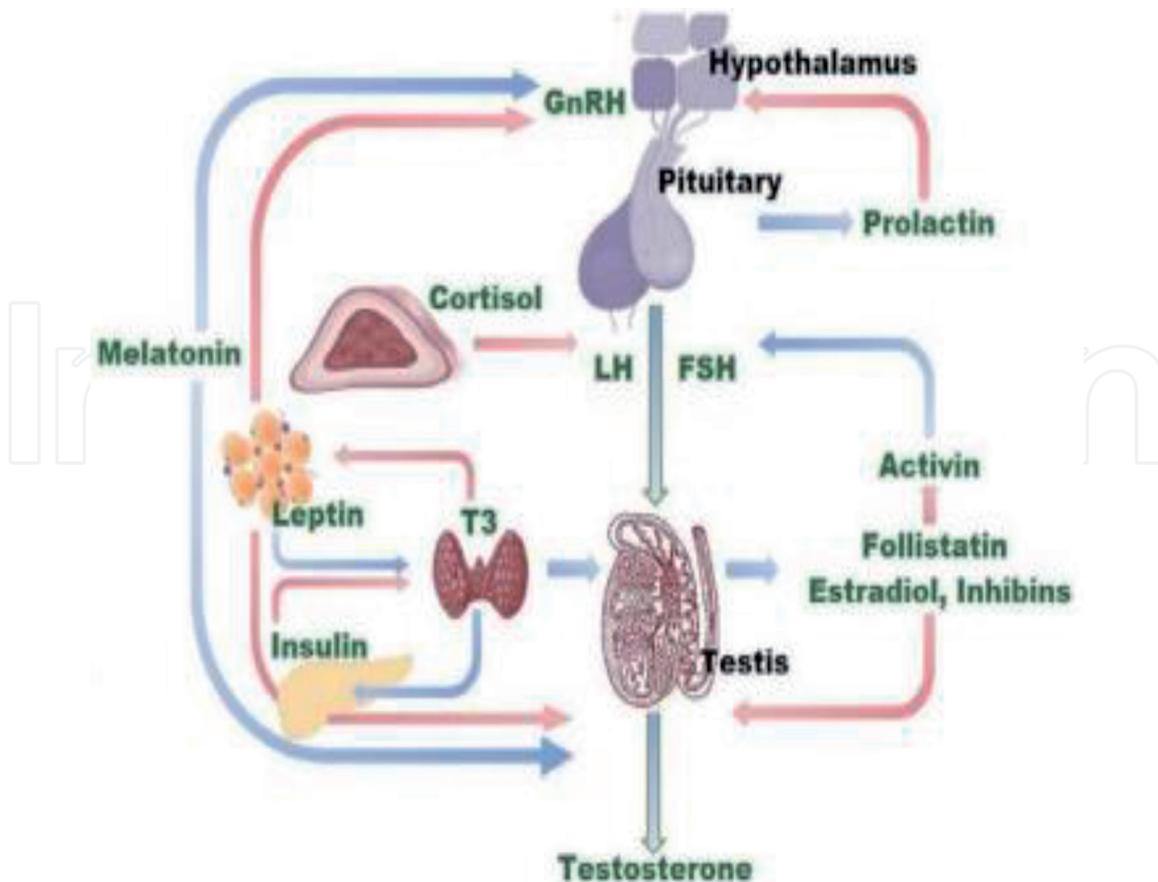


Figure 1. Hypothalamo-pituitary-testicular Axis and its crosstalk with other hormones in the regulation of male reproductive functions [3].

structure of the testes. The hormone, FSH, promotes within seminiferous tubules cell divisions which will result in the production of mature sperm [4].

The luteinizing hormones (LH), also released from pituitary gland, promotes the development of certain endocrine tissues within the testes. These tissues are composed of groups of cells (interstitial tissue) between the seminiferous tubules.

Under the influence of LH, the interstitial tissues secrete the steroid hormone testosterone. Even though testosterone may be secreted by the adrenal cortex, the amount of secretion is usually insignificant [4]. Testosterone is also produced in ovary in females [5].

Testosterone, in the presence of normal amounts of growth hormone, promotes growth of the bony skeleton. This is in addition to promoting male characteristics, male behaviors and the maintenance of the spermatid tubules [4, 6, 9]. The secretion of androgen markedly increases at puberty accounting for rapid growth at that stage of life [4, 7].

Illustration is shown in **Figure 1**.

2.2 Testosterone

Testosterone is the primary male sex hormone and anabolic steroid [6]. It is the main anabolic steroid hormone produced by the body but serving two main effects on the body:

- Anabolic effects, which promote muscle building
- Androgenic effects, which are responsible for male traits, such as facial hair and a deeper voice, among others.

Some athletes take testosterone to boost their performance because of its anabolic effects [6].

Testosterone is produced majorly by the testicles in adult human _ men [7]. In women, the ovaries produce the hormone [8]. The hormone affects a man's appearance and sexual development, stimulates sperm production and regulates a man's sex drive, including semen volume. It also helps build muscles and bone masses [7, 8, 11].

Testosterone production decreases with age. Its production is at its highest in a man's early adulthood and drops slowly each year afterwards [9]. The normal range of testosterone in the body is typically 300 to 1000 ng/dL (nanogram per deciliter). A range of symptoms can occur if its production drastically drops below normal. Men with low testosterone level, also known as 'low T', can experience a range of symptoms if its decrease becomes significant. Low testosterone, or low T, is diagnosed when levels fall severely below 300 ng/dL in male or 15 ng/dL in female. A blood test, called 'a serum testosterone test', is usually used to determine the level of circulating testosterone [7, 9]. When the body does not produce the right amount of testosterone, the condition is called hypogonadism. This is sometimes called "low T". Men diagnosed with hypogonadism can benefit from testosterone therapy. However, therapy is not usually recommended, unless testosterone level falls quite below the normal range for a given age. This is because there are some natural remedies which can help [9].

2.2.1 Normal and abnormal levels of testosterone

A normal testosterone level range for men is 300 to 1000 nanograms per deciliter (ng/dL) [7]. For women, its normal level is between 15 and 70 ng/dL. However, it's also considered normal to have changes in the level of testosterone throughout life [8].

Testosterone levels can decrease naturally due to age or other health conditions. After the age of 40, men's testosterone levels decrease. The decrease, on average, is about one percent (1%) every year. When men reach above 40 years of age, some symptoms of low testosterone become commonly seen. The commonest symptom to appear is erectile dysfunction. Irrespective of age, low testosterone levels have often been observed in people with obesity [8].

Hypogonadism, also called low testosterone, is the most common problem related to testosterone, in men.

As discussed earlier (Section 2.2), Testosterone is responsible for traits such as body hair, muscle mass and strength. Therefore, men with low levels of testosterone might notice a reduction in these traits whereas women with too much testosterone might notice an increase in these traits [8].

2.2.2 Chemical properties of testosterone

The molecular formula is $C_{19}H_{28}O_2$ [10]. The molecular weight is 288.42 g/mol [11]. In medical treatment, the therapeutic testosterone is a synthetic form of endogenous androgenic steroid testosterone [12].

Generally speaking, in vivo, testosterone is converted into dihydrotestosterone (DHT) in the target tissues irreversibly by the enzyme 5-alpha reductase. The testosterone or DHT ligand-androgen receptor complexes then act as transcription factor complexes. In this way, it stimulates the expression of various responsive genes. In comparison, DHT binds with higher affinity to androgen receptors than testosterone, thus activating gene expression more efficiently. Testosterone, in addition, is irreversibly converted to estradiol by the enzyme complex aromatase. This occurs particularly in the liver and adipose tissue. Both testosterone and DHT promote the development and maintenance of male sex traits related to the internal and external genitalia, skeletal muscle and hair follicles. On the other hand, estradiol promotes epiphyseal maturation and bone mineralization. However, because of rapid metabolism by the liver, therapeutic testosterone is generally administered as an ester derivative (Figure 2) [11].



Figure 2.
Chemical structure of testosterone [5].

2.2.3 The role of testosterone

In males, testosterone is the predominant sex hormone [6, 9]. It plays a number of important roles. These roles include;

- a. Development of penis and testes
- b. Deepening of voice at puberty
- c. Appearance of facial and pubic hair at puberty. It starts at puberty but later in life, it may play a role in balding
- d. Building muscle mass and strength
- e. Bone growth and strength
- f. Sex drive (libido)
- g. Sperm production, including semen volume

Therefore, males in adolescent stages of life, who have too little testosterone may not experience normal masculinization. The genitals of such males may not enlarge, as well as their facial and body hair may be scanty. The voice may also not deepen as normally expected [5].

Notably, testosterone also helps in the maintenance of normal mood [7]. Scholars have argued that there may be other important functions of this hormone, testosterone, that have not yet been discovered [5].

To control the production of testosterone in men, signals have to be sent from the hypothalamus in the brain to the pituitary gland at the base of the brain. In turn, the pituitary gland then relays signals to the testes to produce testosterone [4]. Thus, a “feedback loop” closely regulates the amount of this hormone in the blood. Notably, when the level of testosterone rise too high, the brain (hypothalamus) then sends signals to the pituitary to reduce the production [5]. See **Figure 1** about the ‘Hypothalamo-pituitary-testicular Axis’.

For normal working of the ovaries in females, there must be proper balance between testosterone and estrogen. It is a known fact that androgens also play an important role in normal brain functions, including mood, sex drive and cognitive functions, although these areas may still require more studies [1–5].

2.2.4 Too little testosterone

A range of symptoms can occur if testosterone production drastically drops below normal [7]. In past few years, scholars have focused on the effects of testosterone deficiency among men. As already known, that as men grow older, their levels of testosterone drop gradually, about 1–2% each year. The rate of this drop is slower compared to the relatively rapid drop in estrogen in females that culminates in menopause [5]. Majority of men, more than a third, who are above 45 years of age, have reduced levels of testosterone [5].

The following symptoms of deficiency of testosterone in adult males occur: they are but not limited to;

- a. Reduced body and facial hair
- b. Loss of muscle mass
- c. Low libido, impotence, small testicles, reduced sperm count and infertility
- d. Increased breast size
- e. Hot flashes
- f. Irritability, poor concentration and depression
- g. Loss of body hair
- h. Brittle bones and an increased risk of fracture

Indeed some men who have testosterone deficiency have related symptoms or conditions. These symptoms or conditions appear to improve when testosterone replacement is done [4, 5, 9].

Therefore, in a nutshell, men with low levels of testosterone might notice a reduction in body hair, muscle mass and strength, while women with too much testosterone might notice an increase in these traits [8].

2.2.5 Too much testosterone

Having too much naturally-occurring testosterone is not a common problem among men [5]. Too much testosterone is common only in male athletes who inject themselves with the hormone in order to make use of its anabolic effects. This is because anabolic steroids, testosterone or related hormones, increase muscle mass and athletic performance [5].

Thus, problems associated with abnormally high testosterone levels in men include but not limited to;

- a. Low sperm counts, shrinking of the testicles and impotence
- b. Heart muscle damage and increased risk of heart attack
- c. Prostate enlargement with difficulty urinating
- d. Liver disease
- e. Acne
- f. Fluid retention with swelling of the legs and feet
- g. Weight gain, perhaps related in part to increased appetite
- h. High blood pressure and cholesterol
- i. Insomnia
- j. Headaches

k. Increased muscle mass

l. Increased risk of blood clots

m. Stunted growth in adolescents

n. Uncharacteristically aggressive behavior

o. Mood swings, euphoria, irritability, impaired judgment and delusions

On another hand, women with too much testosterone may grow facial hair, develop a deeper voice or experience decreased breast size. Too much testosterone in women can also cause acne [8].

Among women, perhaps the most common cause of a high testosterone level is polycystic ovary syndrome (PCOS). It affects 6–10% of premenopausal women [5, 7].

Therefore, women with too much testosterone might notice an increase in these traits; body hair, muscle mass and strength [8].

2.2.6 Misuse of testosterone in athletes

As already discussed, the effects of testosterone in the body are two; (1) anabolic effects and (2) Virilizing or androgenic effects. Anabolic effects are related to protein synthesis and growth [13]. Male athletes who inject themselves with the hormone in order to make use of its anabolic effects tend to do so to make use of this advantage. This is because anabolic steroids, testosterone or related hormones, increase muscle mass and athletic performance [5]. Anabolic effects involve growth of muscle mass, increased bone density, as well as stimulation of linear growth and bone maturation [13].

Meanwhile, the Virilizing effects, also called androgenic effects, are related to the biological development of male sexual traits. This includes maturation of sex organs, specifically growth of penis and formation of scrotum in male fetus. However, at puberty, testosterone also coordinates development of masculine characteristics such as deepening of the voice and growth of facial hair [13].

2.2.7 Diseases and conditions affecting testosterone

As shown in **Figure 1** about the ‘Hypothalamo-pituitary-testicular Axis’, men will experience drop in testosterone when a disease or condition affects the axis. Thus, conditions or diseases affecting the testes, pituitary and hypothalamus glands also affect testosterone levels in the body.

- Testes – Conditions or disease of testes affecting testosterone include direct injury, castration, infection, radiation treatment, chemotherapy and tumors
- Pituitary and hypothalamus glands – Conditions or disease of pituitary and hypothalamus affecting testosterone include tumors, HIV/AIDS, certain infections and autoimmune conditions and lastly medications. These medications include steroids, morphine or related drugs and major tranquilizers, such as haloperidol, among others.

Klinefelter syndrome and hemochromatosis also affect testosterone levels. Klinefelter syndrome is a genetic disease in which a man has an extra x-chromosome

whereas hemochromatosis is a genetic disease in which an abnormal gene causes excessive iron to accumulate throughout the body. These two conditions can also affect testosterone.

On the other hand, women may have a testosterone deficiency due to diseases of the pituitary, hypothalamus or adrenal glands, in addition to removal of the ovaries [5].

Therefore, high T levels can indicate ovarian or testicular cancer. Low T levels can indicate chronic illness or a problem with the pituitary gland, which releases hormones [8].

2.2.8 Testosterone therapy

Therapy Option: Currently, testosterone therapy is approved primarily for the treatment of delayed male puberty, low production of testosterone and certain inoperable female breast cancers [5].

Testosterone treatment can improve symptoms in men with significantly low levels of active testosterone, such as:

- Generalized weakness
- Low energy
- Disabling frailty
- Depression
- Problems with sexual function
- Problems with cognition.

The most common treatment for low testosterone is testosterone replacement therapy (TRT). TRT is given as an injection, a skin patch, or a topical gel containing testosterone that replaces the testosterone missing from the body [8].

Currently, there is no serious risk from acute poisoning with testosterone replacement therapy but chronic use can cause harm. Major risks of using the hormone are those of excessive androgens [12]. These are menstrual irregularities and virilization in women and impotence, premature cardiovascular disease and prostatic hypertrophy in men. It must be noted that both men and women can suffer liver damage with oral anabolic steroids containing a substituted product, 17-alpha-carbon. Again, psychiatric changes can occur during use or after cessation [12]. TRT falls against the recommendations by American College of Obstetricians and Gynecologists (ACOG) [14].

No Therapy Option: There's no magic solution for boosting testosterone but some natural remedies [9] may help;

- a. Get eight hours night's sleep daily
- b. Lose that excess weight _ weight reduction
- c. Eat food rich with enough Zinc _ Zinc supplements
- d. Reduce dietary sugary intake
- e. Do regular physical exercise

These five remedies can be of help [9].

Eight (8) hours of sleep in every 24 hour is sufficient [9]. However, reduced hours of sleep have tremendous effects on testosterone level [15].

Low levels of testosterone have been discovered in overweight individuals. For this matter, weight reduction is paramount the no therapy option for treating testosterone related problems.

Scholars [9] have coined that men with hypogonadism often have zinc deficiencies. In other literature [16], it is coined that testosterone deficiency is associated with late-onset hypogonadism. Micronutrients [16], such as copper and zinc influence testosterone synthesis. These coupled with reduced dietary sugary intake and regular physical exercise can treat most of your testosterone related problems [9].

2.2.9 Performing testosterone test

A normal testosterone level for men is a range of 300 to 1000 nanograms per deciliter (ng/dL) [7]. For women, its normal level is between 15 and 70 ng/dL. However, it is considered normal to have changes in the level of testosterone throughout life [8].

To have testosterone levels checked requires a simple blood test. The test is usually performed in the morning, when T levels are highest. Sometimes, the test needs to be re-taken to confirm the measurements [8].

Some medications affect testosterone levels and so, the clinician or doctor may require one to stop taking such medication before testosterone test is performed. The medications below can artificially increase testosterone levels. They are;

- Steroids (T levels fall rapidly after one has stopped using steroids)
- Anticonvulsants
- Barbiturates
- Androgen or estrogen therapies

Opiates, in particular, are known to artificially decrease the levels of testosterone [8].

Studies, have confirmed that saliva offers a relatively accurate measurement of testosterone levels. This is especially true when diagnosing male hypogonadism [17]. In an earlier study, it was shown that salivary testosterone, dropped by 47% in 1454 males aged 20-89 years during their life time. However, in a later study (second), it was found that salivary testosterone was strongly correlated with bioavailable testosterone ($p < 0.000001$). It was also strongly correlated with calculated free testosterone ($p < 0.00001$) and total testosterone ($p < 0.002$). Hence forth, salivary testosterone was significantly related to hypogonadal symptoms [17].

However, American College of Obstetricians and Gynecologists Committee (ACOG) and other scholars, recommend against salivary testing for hormone replacement in females [14].

3. Conclusion

Men and women need the proper amount of testosterone to develop and function normally. Checking testosterone levels is quite important. The levels usually vary and for that matter, single low level may not be meaningful, except in the

presence of symptoms related to low T. It is even more meaningless if the level of testosterone was normal at one time. To know when to measure level of testosterone, how best to respond to the results of measurement and when it is necessary to accept the risks of treatment are all areas of more research. Anything less of research might not be helpful.

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Conflict of interest

The author declares no conflict of interest.

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