Al-Ameed Journal for Medical Research and Health Sciences

Volume 1 | Issue 2 Article 1

2023

Testosterone Hormone ; Clinical Indications, Dysregulation and Therapeutic methods

Talal Z. Al-Darawsha
Embryologist in Ministry of Iraqi Heath,Kerbala Health Directorate IRAQ, ttzm20@yahoo.com

Recommended Citation

Al-Darawsha, Talal Z. (2023) "Testosterone Hormone ; Clinical Indications, Dysregulation and Therapeutic methods," *Al-Ameed Journal for Medical Research and Health Sciences*: Vol. 1 : Iss. 2 , Article 1.
Available at: https://doi.org/10.61631/3005-3188.1005

REVIEW

Testosterone Hormone; Clinical Indications, Dysregulation and Therapeutic Methods

Talal Z. Al-Darawsha

Embryologist in Ministry of Iraqi Heath, Iraq

Abstract

Testosterone is a hormone primarily produced by the testicles in adult men and it is the basic male sex hormone and an anabolic steroid. Androgen is important for survival. It is influences a man's appearance and sexual development, stimulating sperm production and regulating sex drive. This hormone is a key growth factor in prostate gland. Prostatic cells stop thriving when testosterone levels fall and Prostate cancer cells shrink both benign and malignant. Testosterone deficiency is a clinical and biochemical syndrome that is linked to ageing and is characterized by typical symptoms and a testosterone deficiency in the blood. The number of people who get it is going up because of ageing and common health problems like obesity, diabetes, and high blood pressure. Several studies have linked a lack of androgen to a higher death rate in men. More and more research links between androgen deficiency and metabolic disorders and effects on lifestyle are being discovered. The aim of the review article was to summarize the latest evidence about the Testosterone hormone in terms of clinical indications and diagnostic tests, as well as the effects of the Testosterone hormone on the different organs in the male human body.

Keywords: Androgen deficiency, Cardiovascular disease, Diabetes, Erectile dysfunction, Metabolic syndrome

Introduction

During embryonic development, testosterone secretion is triggered by the presence of the testis-determining factor (TDF) on the Y chromosome. So that the development of male genitalia, are formed (Vilain et al., 1993).

Both sexes, males and females, communicate their reproductive tissues for the first six weeks of their development. The SRY (sex-related gene on the Y chromosome) kicks off the development of the testicles around week 7 in utero. In the foetal testicles, Sertoli cells develop from the epithelial sex cords of the developing gonads which play role in sperm form morphogenesis (Basaria, 2013a).

In the seventh week of pregnancy, foetal Leydig cells are the source of the initial step in the production of testosterone. The majority of testosterone is produced in the testis by Leydig cells. It is responsible for the production of several different steroids that are necessary for male development. These steroids include estradiol and dihydrotestosterone (Skinner, 2018).

In addition, Male external genitalia and the prostate's growth are stimulated by the conversion of testosterone to dihydrotestosterone. It is also responsible for the testicles' transit through the inguinal canal in the last two months of foetal development (Basaria, 2013b).

Methods

By searching electronic scientific databases Scopus, Science Direct, Springer Link, Pub Med, Google Scholar, and Cochrane Systematic Reviews to include published articles and books from 1975 to 2023.

Functions

1- Testosterone is responsible for basic sexual development, including testicle descent, spermatozoa production, penis and testes hypertrophy, and desire stimulation (Kalfa et al., 2018).
2- Testosterone plays a role in the regulation of secondary male characteristics, including male hair patterns, vocal changes, and a deepening of

Received 21 May 2023; revised 9 June 2023; accepted 6 July 2023.
Available online 16 January 2024
E-mail address: ttzm20@yahoo.com.

https://doi.org/10.61631/3005-3188.1005

the voice. Anabolic effects include growth spurts in puberty (testosterone causes the epiphyseal plate to shut later in puberty) and protein synthesis (testosterone stimulates protein synthesis) and muscularity (Kalfa et al., 2018).

3- Testosterone's ability to stimulate erythropoiesis, males typically have a higher hematocrit percentage than females do. Testosterone levels have a tendency to decrease with increasing age. As a consequence of this, men typically experience a reduction in the size of their testicles, a drop in libido, a decrease in bone density, a decline in muscle mass, an increase in the production of fat, and a reduction in erythropoiesis, which can lead to possible anaemia (Anatomy and Histology of the).

Secretion mechanism

Androgens are secreted by testes. And they are necessary for the maturation of secondary sexual characteristics, libido, and the stimulation of spermatogenesis in males. This is because androgens are essential for the development and function of male reproductive organs and these hormonal cross-tasks affect testicular function, sexual behaviour, and semen quality, including the volume of semen. In addition to this, androgens influence the functioning of a variety of somatic organs (Mooradian et al., 1987).

Hormones can refer to either substances or molecules that are produced by the endocrine system however hormones can be placed into either the protein or steroid category (Dankbar et al., 1995).

Chemically, hormones can be divided into two groups: proteins and steroids. Proteins or protein derivatives make up the majority of hormones, with the exception of those produced by the sex hormones and the adrenal cortex (Hines, 2011).

The hypothalamic-pituitary-gonadal axis plays a significant part in the regulation of testosterone levels and gonadal function during puberty. The hypothalamus is responsible for the production of gonadotropin-releasing hormone (GnRH), which is then transported to the anterior pituitary via the hypothalamohypophyseal portal system. Once there, the anterior pituitary is responsible for the production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Both luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are examples of gonadotropic hormones. These hormones are carried through the blood and bind to receptors in the gonads. In particular, LH acts on the Leydig cells, which causes an increase in the production of testosterone. Through a process known as negative feedback, testosterone is able to inhibit its own secretion. High levels of testosterone in the blood feedback to the hypothalamus, which causes it to suppress the secretion of GnRH. Additionally, high levels of testosterone in the blood stream feedback to the anterior pituitary, which causes it to be less responsive to GnRH stimuli (Bilinska et al., 2009; Plant & Marshall, 2001). See Fig. 1; See Fig. 1; In the setting of the management of reproductive activities in males, the hypothalamic-pituitary-testicular axis and its interactions with other hormones play an important role. Luteinizing hormone means (LH), follicle-stimulating hormone stands for (FSH), and tri-iodothyronine represent (T3). Gonadotropin-releasing hormone stands for (GnRH).

Both luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are necessary for the maturation of testicles as well as the continued operation of the testicles. When it comes to the regulation of Leydig cell functions, LH is by far the most significant hormone. Hormones not only control the size of the Leydig cell population through their control of proliferation and differentiation, but they also regulate steroid production by controlling the metabolic activities that take place in the cells that are already present (Dutta et al., 2019).

Plasma proteins such as sex hormone-binding globulin and albumin bind most of the testosterone in the body. The majority of the protein-bound testosterone serves as a source of extra testosterone for the body. Tissues such as the seminal vesicles, bone, and muscle, as well as the prostate gland, are all affected by the small amounts of free testosterone present in the bloodstream. The enzyme 5-alpha-reductase converts testosterone to dihydrotestosterone at the cellular level (2022Donahue).

Clinical features for testosterone deficiency

In terms of male reproductive health, testosterone is the most important factor. Testosterone is the hormone that is responsible for all of the characteristics that are characteristic of men. Hypogonadism

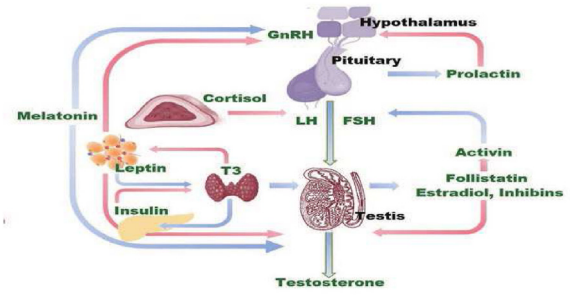

Fig. 1. Hypothalamic-pituitary-testicular axis and hormone overlap in male reproduction (Clark et al., 2018).

is a disorder that affects the whole male organism and is caused when testosterone levels are too low. A shortage of testosterone in male patients is known as hypogonadism. The condition might have a central (pituitary gland or hypothalamic) origin, a testicular origin or a mix of both central and testicular origins (Matsumoto, 2002).

Hypogonadism is a condition that can develop as a consequence of testosterone deficiency, which is linked to a wide range of diseases, particularly mood disorders, cardiovascular diseases, and metabolic syndrome. Symptoms of testosterone deficiency can be very obvious. Hypogonadism is classified into hypergonadotropic hypogonadism or primary hypogonadism when it occurs in male patients who have testicular failure as a result of genetic abnormalities (such as Klinefelter's syndrome), radiation, chemotherapy, orchitis, undescended testes, or trauma. In addition, hypogonadotropic hypogonadism, central hypogonadism, and secondary hypogonadism are all names for the same condition, which describes a weakness or malfunction in the hypothalamic-pituitary axis as a consequence of disease or damage or disease to the axis (Rhoden & Morgentaler, 2004).

Low testosterone levels and high-normal to high levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are seen in people with primary hypogonadism, whereas low testosterone levels and normal to low levels of LH and FSH are seen in patients with secondary hypogonadism (Salonia et al., 2019).

Symptoms of pre-pubertal development include tiny testicles, a small phallus, a reduction in secondary sex characteristics (such as axillary or facial hair), difficulty growing muscular mass, eunuchoid proportions, a low sperm count, gynecomastia, and poor levels of energy and desire. Post-pubertal changes include osteoporosis and hot flashes in those with severe hypogonadism, in addition to the changes that have previously been stated, with the exception of the size and form of the phallus and eunuchoid (Baillargeon et al., 2018) Fig. 2; In target tissues, Testosterone may be transferred to dihydrotestosterone (DHT) in two ways; The first way; 5 a reductase (5aR) isoforms: androgen-independent 5aR type 1 (5aR1) and, The second way; androgen-controlled 5aR type 2. (5aR2), as well as can Testosterone and its precursor, delta-4 androstenedione, may be converted to estrogens via P450 aromatase (ERs).

The role of testosterone in spermatogenesis

Testosterone is the androgen in the testis that initiates and maintains spermatogenesis, and mature sperm generation depends on androgen activity. In the absence of Testosterone or its receptor, spermatogenesis stops at meiosis, causing male sterility (Walker, 2011).

In men, Testosterone is made by Leydig cells when they are stimulated by luteinizing hormone (LH). LH is a glycoprotein hormone that is released from the pituitary gland in response to gonadotropin-releasing hormone (GnRH) pulses from the hypothalamus (Smith & Walker, 2014).

Primary hypogonadism is characterised by the inability of the testis to react to follicle-stimulating hormone (FSH) and luteinizing hormone. When primary hypogonadism inhibits testosterone synthesis, testosterone is inadequate to control FSH and LH production, resulting in increased follicle-stimulating hormone and luteinizing hormone levels (Irvin, 2021).

The pituitary gland secretes gonadotropins, luteinizing hormone, and follicle-stimulating hormone, which encourage Leydig cells to generate testosterone and commence spermatogenesis (Andreassen et al., 2018).

Spermatogenesis is the coordinated series of processes that occurs during the development of spermatogonia into spermatozoa. Differential gene expression and cell-cell interaction are involved in the process, which is controlled by major endocrine stimuli (Andreassen et al., 2018).

Sperm production is increased by the production of androgens (testosterone) in the interstitial cells. and this agent acts on seminiferous tubules by stimulating primary spermatocytes to divide into secondary spermatocytes (Oduwole et al., 2018).

To regulate spermatogenesis, Sertoli cells have receptors for FSH and testosterone and play important role in Neutrietion and developed mental of sperm especially morphogenesis of spermatozoa (Sofikitis et al., 2008). For more illustration, Fig. 3; Follicle-stimulating hormone is the factor that is accountable for the beginning of the process of spermatogenesis. It does this by binding to spermatogonia and Sertoli cells, which in turn stimulates the production of spermatogonia. In addition to this, it stimulates the production of oestrogen as well as an androgen-binding protein by Sertoli cells.

Testosterone and hair

Prior to adolescence, and maturity, male sex hormones are crucial regulators of male bodily development (Werner et al., 2012).

Human hair development is regulated mostly by androgens. A variety of pigmented terminal hair development in both sexes, including pubic and

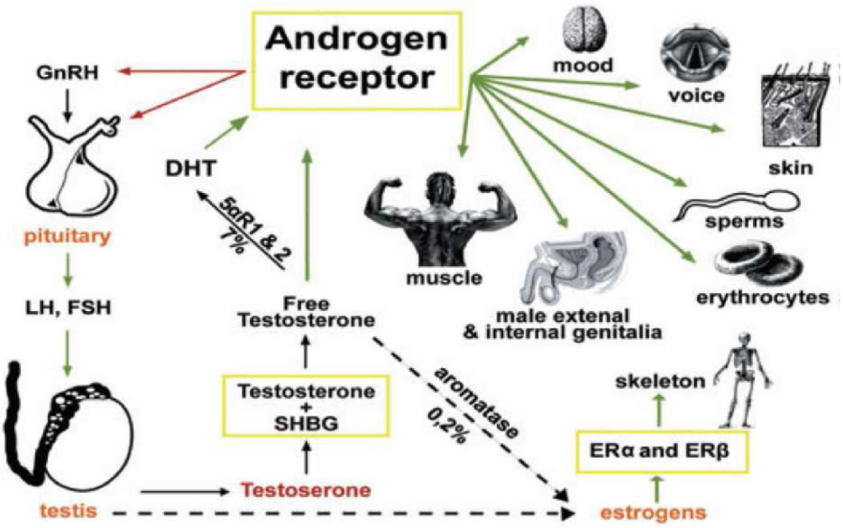

Fig. 2. Testosterone formation and activity in the male body (Corona et al., 2011).

axillary hair and the male beard, is stimulated by these hormones following puberty (Randall et al., 1992).

Androgens cause an increase in the amount of body hair that is evident during puberty (for example, the growth of a beard), and they continue to encourage the growth of various hair follicles and hair sizes for many years (J. B. H. 1958, pp. 399–433).

Androgen-dependent hair diseases, such as hirsutism in women (also known as male pattern hair distribution) and androgenetic alopecia in both sexes, cause considerable psychologic suffering. This is because human hair plays an essential part in the human body's social communication (Randall, 2012).

Androgens function within the follicle to change the interactions between mesenchyme and epithelial cells, which in turn changes the time it takes for hair to develop, the size of the dermal papilla, as well as the activity of keratinocytes, melanocytes, and dermal papilla cells (Androgens, 2008).

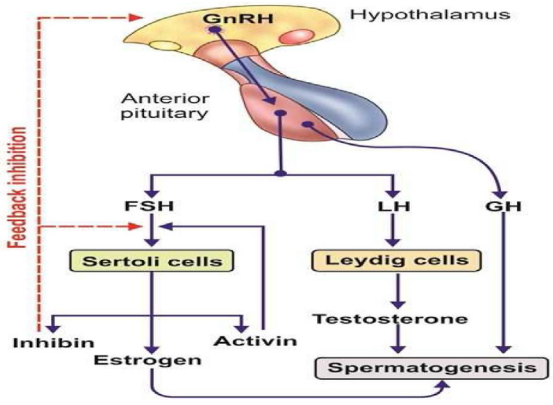

Fig. 3. Role of Testosterone hormones in spermatogenesis in human males (Sembulingam & Prema Sembulingam, 2012).

Testosterone and bone

In males, testosterone is an essential hormone for both the growth of new bone and the preservation of existing bone. Bone growth is faster in hypogonadal males, which leads to an increased risk of fractures. In these males, the treatment of testosterone prevents bone loss and preserves bone mass by inhibiting the process of bone resorption (Sinnesael et al., 2011).

Osteoporosis is a significant and growing health concern, particularly among the elderly. Fractures are a significant burden for society due to the related financial expenditures, morbidity, as well as death rates. Osteoporosis affects a growing number of people (Laurent et al., 2014).

Fragility fractures are the hallmark of senile osteoporosis, which is a kind of osteoporosis that affects elderly men (Boers et al., 1997).

Osteoporosis is a gender-related illness as well: despite the fact that the death rate following hip fracture is greater in men than in women when adjusted for age, fewer males are afflicted by osteoporosis than women (Johnell & Kanis, 2006).

In contrast to postmenopausal women, men do not experience the rapid oestrogen insufficiency that is associated with bone loss. Both of these factors may contribute to the fact that males have larger and, as a result, more robust bones than women do (Seeman et al., 2003).

Testosterone effects on the skeletal muscle

The concept that androgens have anabolic effects on the muscle is not a new one; people have

understood from ancient times that the removal of the testicles causes a decline in a man's vitality (Kochakian, 1975).

Androgens are responsible for the increase in both muscle mass and strength. The resultant increase in physical activity leads to an activation of bone-forming sites, which in turn stimulates osteocytes, the cells responsible for modifying bone production (Notelovitz, 2002).

After men enter their fourth decade of life, their testosterone levels begin to naturally decline at a rate of around one percent every year (Vermeulen et al., 1996). along with a decrease in the strength and mass of the skeletal muscle (Candow & Chilibeck, 2005).

Because of the anabolic properties of testosterone, some sportsmen choose to take it in order to improve their performance (Hartgens & Kuipers, 2004).

Testosterone and cardiovascular disease

The male cardiovascular system (CVS) benefits from normal physiologic levels of testosterone, and testosterone deficiency is associated with an unfavourable metabolic profile and increased Cardiovascular disease events. Normal physiologic levels of testosterone are beneficial to the male cardiovascular system (Elagizi et al., 2018).

Serum testosterone concentrations are known to decline with age, and low testosterone levels have been related to early coronary artery disease, negative effects on Cardiovascular disease risk factors, and an increased risk of cardiovascular death regardless of age (Webb & Collins, 2017).

After accounting for other factors that raise the risk of heart disease, such as smoking and cholesterol levels, the researchers discovered that the risk of clogged arteries is proportional to the amount of testosterone that is present in the body. The lower the testosterone levels, the greater the risk (Malkin et al., 2010).

There is a risk that therapy with testosterone will result in an increase in cholesterol levels. There is a possibility that a heart attack might occur if there is an elevated buildup of cholesterol in the arteries that supply blood to the heart (Morley et al., 1993).

When athletes abuse testosterone and other androgenic steroids, their risk of high blood pressure, heart attack, and stroke increases dramatically. And when taking too much testosterone can hurt high-density lipoprotein (HDL) cholesterol levels and other risk factors for heart disease (Testosterone and the heart, 2010).

In addition, Hormone treatment by testosterone caused a moderate increase in the amount of blood that flowed to the heart muscle by expanding coronary arteries that were otherwise healthy but were not completely occluded. Additionally, testosterone enhanced the contractions of the heart muscle. On the other hand, the medication did not alleviate the discomfort associated with angina, but it did lower high-density lipoprotein cholesterol levels (Vincent et al., 2006).

Testosterone effects on obesity, diabetes and metabolic syndrome

Research conducted in a laboratory setting has demonstrated that testosterone has an effect on fat metabolism mostly through the activation of beta-adrenergic-induced lipolysis. In addition, it has been demonstrated that testosterone inhibits the action of lipoprotein lipase in the adipose tissue found in the abdomen region, which results in a reduction in the amount of triglyceride that is taken up by the central fat depots (Björntorp, 1991).

Men who are obese, have metabolic syndrome, and have type 2 diabetes has been reported to have lower levels of free testosterone, total testosterone, and sex hormone-binding globulin (SHBG). On the other hand, a low level of testosterone and/or sex hormone binding globulin is a risk factor for developing metabolic syndrome as well as type 2 diabetes (Wang et al., 2011).

Men who have low testosterone levels have a greater risk of developing diabetes later in life. In reaction to insulin, testosterone makes it possible for the body's tissues to take in more sugar from the blood. Insulin resistance is more common in men with low testosterone hormone levels; therefore, these men need to create more insulin in order to maintain normal blood sugar levels (Vigen, 2013).

Testosterone and erection dysfunction

Erectile dysfunction is a complex condition, and various emotional, physical, and medical variables contribute to the degree of dysfunction that considerably damages the quality of life of both the patient and partner, which in turn has a negative influence on sexual and reproductive activity (Al-Darawsha et al., 2023).

In men who already suffer from erectile dysfunction due to other circumstances, experts thoughts that low testosterone might substantially contribute, making an already challenging condition even more difficult to manage. So that a low testosterone level is related in some manner with many of the disorders that contribute to erectile dysfunction, one of which is metabolic syndrome (Golden et al., 2009).

Even though there is evidence to show that testosterone plays a significant role in erectile function, it is possible that testosterone levels below the lower limit of the normal range are adequate for the majority of men to maintain regular erections. Nobody really knows how much testosterone has to be circulating in the blood for a man to keep an erection going (Cunningham et al., 2016).

The degree of increases in testosterone and estradiol levels was associated to improvements in sexual desire and activity in response to testosterone therapy in older men with poor libido and low testosterone levels; however, there was no convincing evidence of a threshold effect (Mikhail, 2006).

Testosterone and the prostate gland

The prostate gland is located before the base of the bladder in males of placental animals. This gland is responsible for producing and releasing secretion into the male ejaculate and may be identified by its location (Cunningham et al., 2016). See Fig. 4; shows the position of the prostate in a Human male in a reproductive system and all of the other primary and auxiliary organs.

The prostate is frequently the site of infection and inflammation, and sperm harvested from the epididymis without exposure to the seminal or prostatic fluid can successfully fertilize and give birth. Despite the widespread belief that the prostate plays an important role in protecting the lower urinary tract from infection and in promoting fertility (Fitzpatrick, 2006).

Testosterone is an essential growth factor for the cells that make up the prostate. When there is less testosterone available, the prostate cells cease growing and dividing. A greater drop in the amount of testosterone that is available correlates to a greater loss of prostate cell mass (Silber et al., 1988).

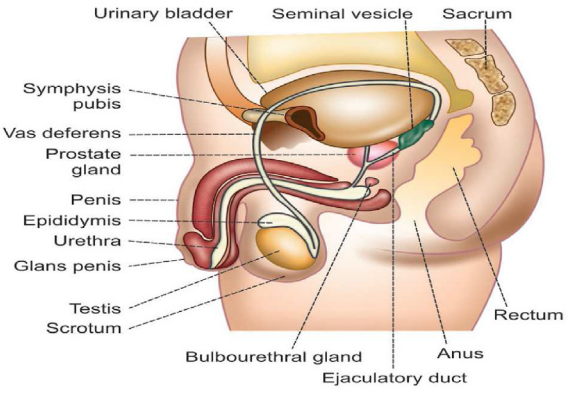

Fig. 4. Male pelvic organs and genitalia (Werner et al., 2012).

Men with the lowest testosterone levels were shown to have a 23% decreased risk of developing prostate cancer compared to the rest of the men. Prostate cancer patients with low testosterone levels had a higher likelihood of developing an aggressive form of the disease, which is worth noting (Bianco, 2008).

However, men who have the greatest amounts of 'free' testosterone are at a larger risk of developing prostate cancer than men who have the lowest levels of testosterone (Watts et al., 2018).

The presence of elevated levels of protein prostate-specific antigen (PSA) may be an indicator of prostate cancer. In addition to this, it may be an indication of illnesses that are not malignant, such as an enlarged prostate or inflammation of the prostate (Cooperberg et al., 2004).

Guidelines on diagnosis and treatment of testosterone deficiency

Males who have low testosterone levels, often known as 'low testosterone,' that refers to when the body does not produce the right amount of testosterone as well as the condition is called hypogonadism. If testosterone levels not enough, the symptoms can become more severe. In men, a diagnosis of low testosterone hormones or low testosterone levels is made when levels decrease significantly below 300 ng/dL, and in females, when levels fall below 15 ng/dL. The amount of testosterone that is circulating in the body is often measured via a blood test that is referred to as a serum testosterone test (Smith, 1996).

The range of testosterone levels that are considered to be normal in the body is normally between 300 and 1000 ng/dL. In the event that its production drops far below normal, a wide variety of symptoms may emerge. Androgen deficiency syndrome in males is a common illness that may cause tiredness, erectile dysfunction, metabolic syndrome, and other clinical symptoms. The amount of testosterone in the blood decreases with age. The frequency of androgen deficiency syndrome in males varies based on the age group, known and unknown comorbidities, and the specific research group. The reported prevalence of androgen insufficiency may be overestimated since not all men with symptoms seek therapy. It's possible that men who complain of androgen insufficiency symptoms are misdiagnosed since the symptoms are so ambiguous (Omona, 2021).

Low testosterone circumstances should be assessed in (Koch et al., 2014).

1- A condition affecting the sellar area, such as a tumour or radiation damage.

Table 1. Lists the possible advantages and disadvantages of testosterone supplementation.

Physiology	Benefits	Harms
Erectile function/libido	Advancement	None
Depression/mood/fatigue	Advancement	Aggressive behaviour
Erythropoiesis	Hematocrit increase	Polycythemia, embolism risk
Skeletal muscle	Fat-free mass increase	None
Bone metabolism	Osteoporosis may be prevented	None
Cardiovascular system	Exercise capacity, congestive heart failure improve	Cardiovascular thromboembolic risk
Prostate		
Benign prostatic hyperplasia	None other than the symptoms of a lack in testosterone.	Prostate-specific antigen levels and volume hardly increased.
Cancer (metastatic or high risk of recurrence)	Absolute contraindication	Repeated occurrences and fast growth
Cancer (localized and treated)	None other than the signs and symptoms of testosterone insufficiency syndrome	Subclinical cancer aggravation
Testicle	None other than the symptoms of a lack in testosterone.	Impairment or atrophy of sperm production

*See Appendix 1 for evidence quality. www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.150033/-/DC1 has Appendix 1.

2- Treatment with medications that affect testosterone production or metabolisms, such as glucocorticoids and opioids
3- Human Immunodeficiency Virus (HIV)
4- End-stage renal disease
5- Chronic obstructive pulmonary disease that ranges from mild to severe.
6- Metabolic syndrome and type 2 diabetes
7- Dysfunction of the erection
8- When the patient is under 40 and experiencing uncommon symptoms like hair loss, weight loss, or acne

The syndrome, often called late-onset hypogonadism, affects older men. Testicular testosterone production is low. Multiple organ systems may be affected, causing serious health problems (Corona et al., 2011).

Testosterone deficiency symptoms are nonspecific, vary in onset and severity, and are not always present. Sexual symptoms and weariness appear first (Buvat et al., 2013). Other symptoms, sadness, sleep disturbances, poor focus, and metabolic diseases (type 2 diabetes, obesity). Age, general health, comorbidities, medicines, a systemic disease, and environmental variables might impact the symptoms. Diagnostics rely heavily on patient history (Hall et al., 2008).

Testosterone replacement therapy is the most common course of action if a problem with low testosterone has been identified. It is worth noting that secondary hypogonadism, which may be treated with pituitary-enhancing medication, is one of the exceptions. It is the ultimate objective of testosterone therapy to alleviate symptoms while also restoring testosterone levels to those seen in healthy young men's eugonadal tissues (Wu et al., 2010).

Table 1; shows the possible benefits and risks of taking extra testosterone (Corona et al., 2013; Cunningham & Toma, 2011).

In males diagnosed with testosterone deficiency syndrome, there are potentially both advantages and risks associated with testosterone supplementation* (Morales et al., 2015).

Symptom improvement should be the main goal, and greater or lower blood testosterone concentrations may be appropriate in people who respond well to therapy (Ruige et al., 2013).

Conclusion

Checking testosterone levels is a critical part of a healthy life. Men and women require testosterone to grow correctly. In men, testosterone has the highest concentration of any circulating androgen from others. It is essential in the diagnosis and ongoing monitoring of a wide variety of disorders, the most notable of which being hypogonadism, and Prostate cells stopped thriving when testosterone levels fall as well as heart failure, type 2 diabetes, erectile dysfunction, and hirsutism in women. Testosterone levels may fluctuate, and one low result may not imply anything unless there are other indications of low testosterone, And more study is needed to determine when and how to test for testosterone levels, how to react to the findings of the test, and whether or not it is essential to accept the dangers of therapy.

Ethics approval and consent to participate

Not need approval.

Consent for publication

Acceptance for publication.

Availability of data and material

For this article review, By searching electronic scientific databases Scopus, Science Direct, Springer Link, Pub Med, Google Scholar, and Cochrane Systematic Reviews to include published articles and books from 1975 to 2023.

Funding

No funding.

Authors' contributions

The author tries to make a substantial and intellectual contribution to the subject research topic.

Conflict of interest

The author declares that there is no conflict of interest.

Acknowledgements

No.

Appendix 1

https://www.cmaj.ca/content/cmaj/suppl/2015/10/26/cmaj.150033.DC1/15-0033-1-at.pdf.

References

Al-Darawsha, T. Z., Dayioglu, N., Al-Azzawi, B. R., & Irez, T. (2023). Can the prediction of intrauterine insemination results by used aniline blue stain (ABS) and sperm chromatin dispersion (SCD) levels? *Advances in Reproductive Sciences, 11*(1), 1–10.

Anatomy and Histology of the pancreas. Pancreapedia: Exocrine Pancreas Knowledge Base.

Andreassen, M., Juul, A., Feldt-Rasmussen, U., & Jørgensen, N. (2018). Semen quality in patients with pituitary disease and adult-onset hypogonadotropic hypogonadism. *Endocrine Connections, 7*(4), 523–533.

Androgens, V. A. R. (2008). *Hair growth* (5th ed.). Dermatologic therapy.

Baillargeon, J., Kuo, Y., Westra, J., Urban, R., & Goodwin, J. (2018). Testosterone prescribing in the United States, 2002-2016. *JAMA, 320*(2), 200.

Basaria, S. (2013a). Reproductive aging in men. *Endocrinology and Metabolism Clinics of North America, 42*(2), 255–270.

Basaria, S. (2013b). Reproductive aging in men. *Endocrinology and Metabolism Clinics, 42*(2), 255–270.

Bianco, F. (2008). Paradigms in androgen/castrate resistant states of prostate cancer in a biomarker era. *Urologic Oncology: Seminars and Original Investigations, 26*(4), 408–414.

Bilinska, B., Kotula-Balak, M., & Sadowska, J. (2009). Morphology and function of human Leydig cells in vitro. Immunocytochemical and radioimmunological analyses. *European Journal of Histochemistry, 53*(1), 5.

Björntorp, P. (1991). Metabolic implications of body fat distribution. *Diabetes Care, 14*(12), 1132–1143.

Boers, M., Verhoeven, A., Markusse, H., van de Laar, M., Westhovens, R., van Denderen, J., et al. (1997). Randomised comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone in early rheumatoid arthritis. *The Lancet, 350*(9074), 309–318.

Buvat, J., Maggi, M., Guay, A., & Torres, L. (2013). Testosterone deficiency in men: Systematic review and standard operating procedures for diagnosis and treatment. *The Journal of Sexual Medicine, 10*(1), 245–284.

Candow, D., & Chilibeck, P. (2005). Differences in size, strength, and power of upper and lower body muscle groups in young and older men. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 60*(2), 148–156.

Clark, B., Prough, R., & Klinge, C. (2018). Mechanisms of action of dehydroepiandrosterone. *Dehydroepiandrosterone*, 29–73.

Cooperberg, M., Lubeck, D., Meng, M., Mehta, S., & Carroll, P. (2004). The changing face of low-risk prostate cancer: Trends in clinical presentation and primary management. *Journal of Clinical Oncology, 22*(11), 2141–2149.

Corona, G., Rastrelli, G., Forti, G., & Maggi, M. (2011). Update in testosterone therapy for men (CME). *The Journal of Sexual Medicine, 8*(3), 639–654.

Corona, G., Rastrelli, G., & Maggi, M. (2013). Diagnosis and treatment of late-onset hypogonadism: Systematic review and meta-analysis of TRT outcomes. *Best Practice & Research Clinical Endocrinology & Metabolism, 27*(4), 557–579.

Cunningham, G., Stephens-Shields, A., Rosen, R., Wang, C., Bhasin, S., Matsumoto, A., et al. (2016). Testosterone treatment and sexual function in older men with low testosterone levels. *Journal of Clinical Endocrinology & Metabolism, 101*(8), 3096–3104.

Cunningham, G., & Toma, S. (2011). Why is androgen replacement in males controversial? *Journal of Clinical Endocrinology & Metabolism, 96*(1), 38–52.

Dankbar, B., Brinkworth, M., Schlatt, S., Weinbauer, G., Nieschlag, E., & Gromoll, J. (1995). Ubiquitous expression of the androgen receptor and testis-specific expression of the FSH receptor in the cynomolgus monkey (Macaca fascicularis) revealed by a ribonuclease protection assay. *The Journal of Steroid Biochemistry and Molecular Biology, 55*(1), 35–41.

Donahue, C. Characteristics of Hormones | SEER Training [Internet]. Training.seer.cancer.gov. 2022 [cited 5 August 2022]. Available from: https://training.seer.cancer.gov/anatomy/endocrine/hormones.html.

Dutta, S., Sengupta, P., & Muhamad, S. (2019). Male reproductive hormones and semen quality. *Asian Pacific Journal of Reproduction, 8*(5), 189.

Elagizi, A., Köhler, T., & Lavie, C. (2018). Testosterone and cardiovascular health. *Mayo Clinic Proceedings, 93*(1), 83–100.

Fitzpatrick, J. (2006). s2wq1. *BJU International, 97*(s2), 3–6.

Golden, S., Robinson, K., Saldanha, I., Anton, B., & Ladenson, P. (2009). Prevalence and incidence of endocrine and metabolic disorders in the United States: A comprehensive review. *Journal of Clinical Endocrinology & Metabolism, 94*(6), 1853–1878.

Hall, S., Esche, G., Araujo, A., Travison, T., Clark, R., Williams, R., et al. (2008). Correlates of low testosterone and symptomatic androgen deficiency in a population-based sample. *Journal of Clinical Endocrinology & Metabolism, 93*(10), 3870–3877.

Hartgens, F., & Kuipers, H. (2004). Effects of androgenic-anabolic steroids in athletes. *Sports Medicine, 34*(8), 513–554.

Hines, M. (2011). Prenatal endocrine influences on sexual orientation and on sexually differentiated childhood behavior. *Frontiers in Neuroendocrinology, 32*(2), 170–182.

H, J. B. (1958). *Age, sex, and genetic factors in the regulation of hair growth in man: a comparison of Caucasian and Japanese populations* (pp. 399–433). Academic Press.

Irvin, H. (2021). *Male Hypogonadism - Genitourinary Disorders - MSD Manual Professional Edition [Internet]*. MSD Manual Professional Edition. Available from: https://www.msdmanuals.com/professional/genitourinary-disorders/male-

reproductive-endocrinology-and-related-disorders/male-hypogonadism.
Johnell, O., & Kanis, J. (2006). An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporosis International, 17*(12), 1726–1733.
Kalfa, N., Gaspari, L., Ollivier, M., Philibert, P., Bergougnoux, A., Paris, F., et al. (2018). Molecular genetics of hypospadias and cryptorchidism recent developments. *Clinical Genetics, 95*(1), 122–131.
Kochakian, C. (1975). Definition of androgens and protein anabolic steroids. *Pharmacology & Therapeutics - Part B: General and Systematic Pharmacology, 1*(2), 149–177.
Koch, C., Ullah, M., & Riche, D. (2014). Transdermal testosterone replacement therapy in men. *Drug Design, Development and Therapy*, 101.
Laurent, M., Sinnesael, M., Vanderschueren, D., Antonio, L., Classens, F., Dubois, V., et al. (2014). Androgens and estrogens in skeletal sexual dimorphism. *Asian Journal of Andrology, 16*(2), 213.
Malkin, C., Pugh, P., Morris, P., Asif, S., Jones, T., & Channer, K. (2010). Low serum testosterone and increased mortality in men with coronary heart disease. *Heart, 96*(22), 1821–1825.
Matsumoto, A. (2002). Andropause: Clinical implications of the decline in serum testosterone levels with aging in men. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 57*(2), M76–M99.
Mikhail, N. (2006). Does testosterone have a role in erectile function? *The American Journal of Medicine, 119*(5), 373–382.
Mooradian, A., Morley, J., & Korenman, S. (1987). Biological actions of androgens. *Endocrine Reviews, 8*(1), 1–28.
Morales, A., Bebb, R., Manjoo, P., Assimakopoulos, P., Axler, J., Collier, C., et al. (2015). Diagnosis and management of testosterone deficiency syndrome in men: Clinical practice guideline. *Canadian Medical Association Journal, 187*(18), 1369–1377.
Morley, J., Perry, H., Kaiser, F., Kraenzle, D., Jensen, J., Houston, K., et al. (1993). Effects of testosterone replacement therapy in old hypogonadal males: A preliminary study. *Journal of the American Geriatrics Society, 41*(2), 149–152.
Notelovitz, M. (2002). Androgen effects on bone and muscle. *Fertility and Sterility, 77*, 34–41.
Oduwole, O., Peltoketo, H., & Huhtaniemi, I. (2018). Role of follicle-stimulating hormone in spermatogenesis. *Frontiers in Endocrinology, 9*.
Omona, K. (2021). *Testosterone*. Reproductive Hormones.
Plant, T., & Marshall, G. (2001). The functional significance of FSH in spermatogenesis and theControl of its secretion in male primates. *Endocrine Reviews, 22*(6), 764–786.
Randall, V. (2012). Androgens and hair: A biological paradox with clinical consequences. *Testosterone*, 154–176.
Randall, V., Thornton, M., Hamada, K., & Messenger, A. (1992). Mechanism of androgen action in cultured dermal papilla cells derived from human hair follicles with varying responses to androgens in vivo. *Journal of Investigative Dermatology, 98*(6), S86–S91.
Rhoden, E., & Morgentaler, A. (2004). Risks of testosterone-replacement therapy and recommendations for monitoring. *New England Journal of Medicine, 350*(5), 482–492.
Ruige, J., Ouwens, D., & Kaufman, J. (2013). Beneficial and adverse effects of testosterone on the cardiovascular system in men. *Journal of Clinical Endocrinology & Metabolism, 98*(11), 4300–4310.
Salonia, A., Rastrelli, G., Hackett, G., Seminara, S., Huhtaniemi, I., Rey, R., et al. (2019). Paediatric and adult-onset male hypogonadism. *Nature Reviews Disease Primers, 5*(1).
Seeman, T., Dubin, L., & Seeman, M. (2003). Religiosity/spirituality and health: A critical review of the evidence for biological pathways. *American Psychologist, 58*(1), 53–63.
Sembulingam, K., & Prema Sembulingam, P. (2012). Essentials of medical physiology. In *New Delhi • Panama city • London • dhaka • kathmandu* (6th ed.). JAYPEE BROTHERS MEDICAL PUBLISHERS (P) LTD.
Silber, S., Balmaceda, J., Borrero, C., Ord, T., & Asch, R. (1988). Pregnancy with sperm aspiration from the proximal head of the epididymis: A new treatment for congenital absence of the vas deferens. *Fertility and Sterility, 50*(3), 525–528.
Sinnesael, M., Boonen, S., Claessens, F., Gielen, E., & Vanderschueren, D. (2011). Testosterone and the male skeleton: A dual mode of action. *Journal of Osteoporosis, 2011*, 1–7.
Skinner, M. K. (2018 Jun 29). *Encyclopedia of reproduction*. Academic Press.
Smith, D. (1996). Longitudinal screening for prostate cancer with prostate-specific antigen. *JAMA, the Journal of the American Medical Association, 276*(16), 1309.
Smith, L., & Walker, W. (2014). The regulation of spermatogenesis by androgens. *Seminars in Cell & Developmental Biology, 30*, 2–13.
Sofikitis, N., Giotitsas, N., Tsounapi, P., Baltogiannis, D., Giannakis, D., & Pardalidis, N. (2008). Hormonal regulation of spermatogenesis and spermiogenesis. *The Journal of Steroid Biochemistry and Molecular Biology, 109*(3–5), 323–330.
[Internet]. *Testosterone and the heart - harvard health* (2010). Harvard Health [cited 24 August 2022]. Available from: https://www.health.harvard.edu/heart-health/testosterone-and-the-heart.
Vermeulen, A., Kaufman, J., & Giagulli, V. (1996). Influence of some biological indexes on sex hormone-binding globulin and androgen levels in aging or obese males. *Journal of Clinical Endocrinology & Metabolism, 81*(5), 1821–1826.
Vigen, R. (2013). Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. *JAMA, 310*(17), 1829.
Vilain, E., Jaubert, F., Fellous, M., & McElreavey, K. (1993). Pathology of 46, XY pure gonadal dysgenesis: Absence of testis differentiation associated with mutations in the testis-determining factor. *Differentiation, 52*(2), 151–159.
Vincent, M., Clerk, L., Lindner, J., Price, W., Jahn, L., Leong-Poi, H., et al. (2006). Mixed meal and light exercise each recruit muscle capillaries in healthy humans. *American Journal of Physiology - Endocrinology And Metabolism, 290*(6), E1191–E1197.
Walker, W. (2011). Testosterone signaling and the regulation of spermatogenesis. *Spermatogenesis, 1*(2), 116–120.
Wang, C., Jackson, G., Jones, T., Matsumoto, A., Nehra, A., Perelman, M., et al. (2011). Low testosterone associated with obesity and the metabolic syndrome contributes to sexual dysfunction and cardiovascular disease risk in men with type 2 diabetes. *Diabetes Care, 34*(7), 1669–1675.
Watts, E., Appleby, P., Perez-Cornago, A., Bueno-de-Mesquita, H., Chan, J., Chen, C., et al. (2018). Low free testosterone and prostate cancer risk: A collaborative analysis of 20 prospective studies. *European Urology, 74*(5), 585–594.
Webb, C., & Collins, P. (2017). Role of testosterone in the treatment of cardiovascular disease. *European Cardiology Review, 12*(2), 1.
Werner, R., Bunch, T., Hiort, O., & Hughes, I. (2012). Androgen insensitivity syndrome. *Seminars in Reproductive Medicine, 30*(5), 432–442.
Wu, F., Tajar, A., Beynon, J., Pye, S., Silman, A., Finn, J., et al. (2010). Identification of late-onset hypogonadism in middle-aged and elderly men. *New England Journal of Medicine, 363*(2), 123–135.