GENETRACK Diagnostics

Testosterone, Total and Free

WHAT IS TESTOSTERONE?

Testosterone is the primary sex hormone in males, but it is also important in females. Testosterone is secreted from the testicles in males, and from the ovaries in females (1).

PURPOSE OF A TESTOSTERONE TEST

In males, a testosterone test may be required for:

- Determining the cause of infertility
- Evaluating a lack of sex drive or ability to get and sustain an erection
- Monitoring the effect of testosterone therapy (for males with low testosterone) and testosterone-lowering medicines (such as males being treated for advanced prostate cancer)
- Finding out the cause of osteoporosis

In females, a testosterone test may be required for:

- Determining why male characteristics are present (e.g., deep voice and excessive facial and body hair)
- Finding the cause of irregular menstrual periods

TOTAL VERSUS FREE TESTOSTERONE

In the circulation, approximately 97% of testosterone is transported by proteins, in particular the sex hormone-binding globulin (SHBG), and also weakly bound to albumin. Only the remaining small fraction of testosterone is circulating in the free form, and it is this free testosterone that is considered the active fraction (2).

REFERENCE RANGES FOR TESTOSTERONE

Males from 18 to 39 years typically have total testosterone levels of 229 – 902 ng/dL and free testosterone levels of 20 – 293 pg/mL with total and free testosterone levels gradually decreasing with age (3).

Testosterone levels in females are a lot lower, with normal total testosterone levels of 8 – 60 ng/d/L, and free testosterone levels typically 1 – 8.5 pg/mL (4).

ROLES OF TESTOSTERONE

Testosterone has an important role during the life cycle of both males and females. Testosterone levels before birth are associated with sex formation (5), potentially brain masculinization during early infancy (6), and pubertal effects, including penis or clitoris enlargement, increased libido, remodelling of facial bones, acne, pubic hair, and deepening of voice (7).

In adult males, testosterone is necessary for normal sperm development, enhances muscle growth, and regulates platelet aggregation (8, 9). In females, testosterone also enhances muscle and bone growth, may modulate the physiology of vaginal tissue, and contributes to female genital sexual arousal (10).

TESTOSTERONE AND METABOLISM

Variations in testosterone levels also influence metabolic parameters, particularly in the control of glucose and energy metabolism (11). In males, low serum testosterone levels are associated with an adverse metabolic profile, including an increased risk of insulin resistance (12), obesity and type 2 diabetes (13).

In contrast, high free testosterone levels in females are associated with increased risk of elevated BMI, insulin resistance and type 2 diabetes (14, 15).

LOW TESTOSTERONE IN MALES

Low testosterone is defined by the American Urology Association as total blood testosterone levels less than 300 ng/dL. Symptoms of low testosterone can include low sex drive, fatigue, reduced lean muscle mass, irritability, erectile dysfunction, infertility, weight gain, osteoporosis, and depression (16).

Low testosterone can occur due to conditions that males are born with, such as Klinefelter syndrome. Testosterone levels may also decline for other reasons, including testicle injury, chemotherapy, infection, autoimmune disease, malnutrition, and hormonal imbalances. Testosterone therapy is available for men with low testosterone levels, although often other changes, such as more physical exercise for overweight men, can increase testosterone levels (16).

HIGH TESTOSTERONE IN MALES

Elevated testosterone in males is not a common problem, and is most often observed in athletes who use anabolic steroids, testosterone, or related hormones to increase muscle mass and athletic performance. Elevated testosterone can cause many health complications, including low sperm counts, impotence, liver disease, acne, blood clots, aggressive behaviour, damage to heart tissue, weight gain, mood swings, excessive body hair, and sleep apnea (17).

TESTOSTERONE AND FERTILITY IN WOMEN

In healthy women, testosterone briefly increases mid menstrual cycle to coincide with ovulation and the most fertile period of the cycle. Testosterone helps to promote the development of follicles, which hold and release eggs during ovulation (18). The correct level of testosterone is important, as both too much or too little can interfere with female fertility.

The signs of reduced testosterone include low muscle mass, poor sleep, lack of energy, depression, low libido, and vaginal dryness. Excess testosterone can lead to acne, polycystic ovary syndrome, irregular menstruation, increased body hair, and low HDL (good) cholesterol.

TEST PROCEDURE

Correct specimen collection and handling is required for optimal assay performance.

This test requires a blood sample from a finger prick. All supplies for sample collection are provided in this kit. First wash and dry hands. Warm hands aid in blood collection. Clean the finger prick site with the alcohol swab and allow to air dry. Use the provided lancet to puncture the skin in one quick, continuous and deliberate stroke. Wipe away the first drop of blood. Massage hand and finger to increase blood flow to the puncture site. Angle arm and hand downwards to facilitate blood collection on the fingertip. Drip blood onto the blood collection card or into the microtainer tube.

Avoid squeezing or 'milking' the finger excessively. If blood flow stops, perform a second skin puncture on another finger, if more blood is required. Do not touch the fingertip.

Dispose of all sharps safely and return sample to the laboratory in the provided prepaid return shipping envelope.

Upon receipt at the laboratory, the blood sample is analyzed by three assays:

- Alinity i 2nd Generation Testosterone assay
- Alinity i SHBG assay
- Alinity c Albumin BCP assay

The testosterone assay measures total testosterone levels by binding to monoclonal anti-testosterone coated microparticles. The amount of testosterone in the blood sample is measured in relative light units by a chemiluminescent reaction.

The SHBG assay measures sex hormone binding globulin (SHBG) levels by binding to monoclonal anti-SHBG coated microparticles. The amount of SHBG in the blood sample is measured in relative light units by a chemiluminescent reaction.

The albumin assay measures albumin levels using colorimetric methodology, where bromcresol purple specifically binds to albumin to produce a coloured complex.

Free testosterone levels are calculated using the Vermeulen equation (13).

TEST INTERPRETATION

This assay will provide accurate free testosterone values for the tested specimen. This value is to be used in conjunction with other clinical and laboratory information for analyses of general health and fertility.

DISCLAIMERS/LIMITATIONS

Certain medications, (including estrogen, some pain medicines, and some seizure medicines), can influence testosterone levels. Long-term excessive alcohol consumption is associated with lower testosterone levels. Thyroid disorders can also affect SHBG levels, leading to overall changes in total testosterone.

These results should be interpreted in conjunction with other laboratory and clinical information.

Assay interference may occur in specimens from individuals routinely exposed to animals or to animal serum products. Additional clinical or diagnostic information may be required for these specimens.

Additional testing is recommended if testosterone results are inconsistent with clinical evidence.

False results may occur in specimens from individuals that have received preparations of mouse monoclonal antibodies for diagnosis or therapy. Additional clinical or diagnostic information may be required for these specimens.

This assay cannot be used for specimens from patients receiving Nandrolone treatment.

Correct specimen collection and handling is required for optimal assay performance. The assay is unaffected (≤10% interference) by hemoglobin (100 mg/dL), bilirubin (15 mg/dL), triglycerides (1000 mg/dL), biotin (30 ng/mL), and protein (12 g/dL).

REFERENCES

(1) Torjesen PA, & Sandnes L. (2004). Serum testosterone in women as measured by an automated immunoassay and a RIA. *Clin Chem*, 50 (3), 678.

(2) Dunn JF, Nisula BC, & Rodbard D. (1981). Transport of Steroid Hormones: Binding of 21 Endogenous Steroids to Both Testosterone-Binding Globulin and Corticosteroid-Binding Globulin in Human Plasma. *J Clin Endocrin Metab*, 53, 58-68.

(3) Travison TG, et al. Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe. J Clin Endocrinol Metab. 2017 Apr 1;102(4):1161-1173.

(4) 2. Rifai N, Horvath AR, & Wittwer C. (2018). Tietz textbook of clinical chemistry and molecular diagnostics (Sixth edition.). St. Louis, Missouri: Elsevier.

(5) Swaab DF, & Garcia-Falgueras A. (2009). Sexual differentiation of the human brain in relation to gender identity and sexual orientation. *Funct Neurol, 24* (1), 17-28.

(6) Dakin CL, et al. (2008). Neonatal stimulation of 5-HT(2) receptors reduces androgen receptor expression in the rat anteroventral periventricular nucleus and sexually dimorphic preoptic area. *Eur J Neurosci, 27* (9), 2473-2480.

(7) Raggatt LJ, & Partridge NC. (2010). Cellular and molecular mechanisms of bone remodeling . *J Biol Chem, 285* (33), 25103-25108.

(8) Ajayi AA, Mathur R, & Halushka PV. (1995). Testosterone increases human platelet thromboxane A2 receptor density and aggregation responses. *Circulation, 91* (11), 2742-2747.

(9) Mehta PH, Jones AC, & Josephs RA. (2008). The social endocrinology of dominance: basal testosterone predicts cortisol changes and behavior following victory and defeat. *J Pers Soc Psychol, 94* (6), 1078-1093.

(10) Traish AM, et al. (2002). Role of androgens in female genital sexual arousal: receptor expression, structure, and function. *Fertil Steril, 77* (Suppl 4), S11-S18.

(11) Navarro G, et al. (2015). The role of androgens in metabolism, obesity, and diabetes in males and females. *Obesity.* 23(4).

(12) Pitteloud N, et al. (2005). Relationship Between Testosterone Levels, Insulin Sensitivity, and Mitochondrial Function in Men. *Diabetes Care.* 28(7), 1636-1642.

(13) Dhindsa S, et al. (2010). Testosterone Concentrations in Diabetic and Nondiabetic Obese Men. *Diabetes Care.* 33(6), 1186-1192.

(14) Kim SY, et al. (1993). Direct Relationship between Elevated Free Testosterone and Insulin Resistance in Hyperprolactinemic Women. *Korean J Intern Med.* 8(1), 8-14.

(15) Antonio L, et al. (2018). Free Testosterone Reflects Metabolic as well as Ovarian Disturbances in Subfertile Oligomenorrheic Women. *Int J Endocrinol.* 2018, 7956951.

(16) What is Low Testosterone? *Urology Care Foundation.*

(17) Testosterone – What It Does And Doesn't Do. (2019). *Harvard Health Publishing, Harvard Medical School.*

(18) Sen A, et al. (2014). Androgens regulate ovarian follicular development by increasing follicle stimulating hormone receptor and microRNA-125b expression. PNAS, 11