
Overview

Useful For

Evaluation of men with symptoms or signs of possible hypogonadism, such as loss of libido, erectile dysfunction, gynecomastia, osteoporosis, or infertility

Evaluation of boys with delayed or precocious puberty

Monitoring testosterone replacement therapy

Monitoring antiandrogen therapy (eg, used in prostate cancer, precocious puberty, treatment of idiopathic hirsutism, male-to-female transgender disorders, etc.)

Evaluation of women with hirsutism, virilization, and oligoamenorrhea

Evaluation of women with symptoms or signs of possible testosterone deficiency

Evaluation of infants with ambiguous genitalia or virilization

Diagnosis of androgen-secreting tumors

Testing Algorithm

See [Steroid Pathways](#) in Special Instructions

Special Instructions

- [Steroid Pathways](#)

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

Portions of this test are covered by patents held by Quest Diagnostics

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Necessary Information

Patient's age and sex are required.

Specimen Required

Container/Tube: Red top (serum gel/SST are **not** acceptable)

Specimen Volume: 1 mL

Forms

If not ordering electronically, complete, print, and send a [General Request](#) (T239) with the specimen.

Specimen Minimum Volume

0.215 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	14 days	
	Frozen	60 days	

Clinical & Interpretive**Clinical Information**

Testosterone is the major androgenic hormone. It is responsible for the development of the male external genitalia and secondary sexual characteristics. In females, its main role is as an estrogen precursor. In both genders, it exerts anabolic effects and influences behavior.

In males, testosterone is secreted by the testicular Leydig cells and, to a minor extent, by the adrenal cortex. In premenopausal women, the ovaries are the main source of testosterone with minor contributions by the adrenal glands and peripheral tissues. After menopause, ovarian testosterone production is significantly diminished. Testosterone production in testes and ovaries is regulated via pituitary-gonadal feedback involving luteinizing hormone (LH) and, to a lesser degree, inhibins and activins.

Most circulating testosterone is bound to sex hormone-binding globulin (SHBG), which, in males, is also called testosterone-binding globulin. A lesser fraction is albumin bound and a small proportion exists as free hormone. Historically, only free testosterone was thought to be the biologically active component. However, testosterone is weakly bound to serum albumin and dissociates freely in the capillary bed, thereby becoming readily available for tissue uptake. All non-SHBG-bound testosterone is therefore considered bioavailable.

During childhood, excessive production of testosterone induces premature puberty in boys and masculinization in girls. In adult women, excess testosterone production results in varying degrees of virilization, including hirsutism, acne, oligomenorrhea, or infertility. Mild-to-moderate testosterone elevations are usually asymptomatic in males but can cause distressing symptoms in females. The exact cause for mild-to-moderate elevations of testosterone often remains obscure. Common causes of pronounced elevations include genetic conditions (eg, congenital adrenal hyperplasia), adrenal, testicular, and ovarian tumors, and abuse of testosterone or gonadotrophins by athletes.

Decreased testosterone in females causes subtle symptoms. These may include some decline in libido and nonspecific mood changes. In males, it results in partial or complete degrees of hypogonadism. This is characterized by changes in male secondary sexual characteristics and reproductive function. The cause is either primary or secondary/tertiary (pituitary/hypothalamic) testicular failure. In adult males, there also is a gradual modest but progressive decline in testosterone production starting between the fourth and sixth decade of life. Since this is associated with a simultaneous increase of SHBG levels, bioavailable testosterone may decline more significantly than apparent total testosterone, causing nonspecific symptoms similar to those observed in testosterone deficient females. However, severe hypogonadism, consequent to aging alone, is rare.

Measurement of total testosterone is often sufficient for diagnosis, particularly if it is combined with measurements of LH and follicle-stimulating hormone (LH / Luteinizing Hormone [LH], Serum and FSH / Follicle-Stimulating Hormone [FSH], Serum). However, these tests may be insufficient for diagnosis of mild abnormalities of testosterone homeostasis, particularly if abnormalities in SHBG (SHBG / Sex Hormone-Binding Globulin [SHBG], Serum) function or levels are present. Additional measurements of bioavailable (TTBS / Testosterone, Total and Bioavailable, Serum) or free testosterone (TGRP / Testosterone Total and Free, Serum) are recommended in this situation.

See [Steroid Pathways](#) in Special Instructions.

Reference Values

Males

0-5 months: 75-400 ng/dL

6 months-9 years: <7-20 ng/dL

10-11 years: <7-130 ng/dL

12-13 years: <7-800 ng/dL

14 years: <7-1,200 ng/dL

15-16 years: 100-1,200 ng/dL

17-18 years: 300-1,200 ng/dL

> or =19 years: 240-950 ng/dL

Tanner Stages*

I (prepubertal): <7-20

II: 8-66

III: 26-800

IV: 85-1,200

V (young adult): 300-950

Females

0-5 months: 20-80 ng/dL

6 months-9 years: <7-20 ng/dL

10-11 years: <7-44 ng/dL

12-16 years: <7-75 ng/dL

17-18 years: 20-75 ng/dL

> or =19 years: 8-60 ng/dL

Tanner Stages*

I (prepubertal): <7-20

II: <7-47

III: 17-75

IV: 20-75

V (young adult): 12-60

*Puberty onset (transition from Tanner stage I to Tanner stage II) occurs for boys at a median age of 11.5 (+/-2) years and for girls at a median age of 10.5 (+/-2) years. There is evidence that it may occur up to 1 year earlier in obese girls and in African American girls. For boys, there is no definite proven relationship between puberty onset and body weight or ethnic origin. Progression through Tanner stages is variable. Tanner stage V (young adult) should be reached by age 18.

Interpretation

In males:

Decreased testosterone levels indicate partial or complete hypogonadism. In hypogonadism, serum testosterone levels are usually below the reference range. The cause is either primary or secondary/tertiary (pituitary/hypothalamic) testicular failure.

Primary testicular failure is associated with increased luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, and decreased total, bioavailable, and free testosterone levels. Causes include:

- Genetic causes (eg, Klinefelter syndrome, XXY males)
- Developmental causes (eg, testicular maldescent)
- Testicular trauma or ischemia (eg, testicular torsion, surgical mishap during hernia operations)
- Infections (eg, mumps)
- Autoimmune diseases (eg, autoimmune polyglandular endocrine failure)
- Metabolic disorders (eg, hemochromatosis, liver failure)
- Orchidectomy

Secondary/tertiary hypogonadism, also known as hypogonadotropic hypogonadism, shows low testosterone and low, or inappropriately "normal" LH/FSH levels. Causes include:

- Inherited or developmental disorders of hypothalamus and pituitary (eg, Kallmann syndrome, congenital hypopituitarism)
- Pituitary or hypothalamic tumors
- Hyperprolactinemia of any cause
- Malnutrition
- Excessive exercise
- Cranial irradiation
- Head trauma

-Medical or recreational drugs (eg, estrogens, gonadotropin releasing hormone [GnRH] analogs, cannabis)

Increased testosterone levels:

-In prepubertal boys, increased levels of testosterone are seen in precocious puberty. Further workup is necessary to determine the cause of precocious puberty.

-In adult males, testicular or adrenal tumors or androgen abuse might be suspected if testosterone levels exceed the upper limit of the normal range by more than 50%.

Monitoring of testosterone replacement therapy:

Aim of treatment is normalization of serum testosterone and LH. During treatment with depot-testosterone preparations, trough levels of serum testosterone should still be within the normal range, while peak levels should not be significantly above the normal young adult range.

Monitoring of antiandrogen therapy:

Aim is usually to suppress testosterone levels to castrate levels or below (no more than 25% of the lower reference range value, typically <50% ng/dL).

In females:

Decreased testosterone levels may be observed in primary or secondary ovarian failure, analogous to the situation in men, alongside the more prominent changes in female hormone levels. Most women with oophorectomy have a significant decrease in testosterone levels.

Increased testosterone levels may be seen in:

-Congenital adrenal hyperplasia. Non-classical (mild) variants may not present in childhood, but during or after puberty. In addition to testosterone, multiple other androgens or androgen precursors, such as 17 hydroxyprogesterone (OHPG / 17-Hydroxyprogesterone, Serum), are elevated, often to a greater degree than testosterone.

-Analogous to males, but at lower levels in prepubertal girls, increased levels of testosterone are seen in precocious puberty.

-Ovarian or adrenal neoplasms. High estrogen values also may be observed and LH and FSH are low or "normal." Testosterone-producing ovarian or adrenal neoplasms often produce total testosterone values above 200 ng/dL.

-Polycystic ovarian syndrome. Hirsutism, acne, menstrual disturbances, insulin resistance and, frequently, obesity form part of this syndrome. Total testosterone levels may be normal or mildly elevated and uncommonly above 200 ng/dL.

Monitoring of testosterone replacement therapy:

The efficacy of testosterone replacement in females is under study. If it is used, then levels should be kept within the normal female range at all times. Bioavailable (TTBS / Testosterone, Total and Bioavailable, Serum) or free testosterone (TGRP / Testosterone, Total and Free, Serum) levels should also be monitored to avoid overtreatment.

Monitoring of antiandrogen therapy:

Antiandrogen therapy is most commonly employed in the management of mild-to-moderate idiopathic female hyperandrogenism, as seen in polycystic ovarian syndrome. Total testosterone levels are a relatively crude guideline for therapy and can be misleading. Therefore, bioavailable (TTBS / Testosterone, Total and Bioavailable, Serum) or free testosterone (TGRP / Testosterone, Total and Free, Serum) also should be monitored to ensure treatment adequacy. However, there are no universally agreed biochemical end points and the primary treatment end point is the clinical

response.

See [Steroid Pathways](#) in Special Instructions.

Cautions

Early-morning testosterone levels in young male individuals are on average 50% higher than p.m. levels. Reference ranges were established using specimens collected in the morning.

Testosterone levels can fluctuate substantially between different days, and sometimes even more frequently. Assessment of androgen status should be based on more than a single measurement.

The low end of the normal reference range in pre-pubertal subjects is not yet established due to sensitivity limitations of current assay methodologies.

Supportive Data

While, particularly at low testosterone concentrations, interferences, cross-reactivity, and lack of result comparability between different assays have bedeviled testosterone immunoassays, this current method is based on liquid chromatography-tandem mass spectrometry and provides reproducible and highly accurate testosterone measurements throughout the analytical range. Therefore, results will be lower than, and not directly comparable with, results obtained by immunoassays. Most immunoassays overestimate the true testosterone concentration by 10% to 300%, depending on the assay used and whether the measured concentration falls into the low, medium, or high range.

Clinical Reference

1. Manni A, Pardridge WM, Cefalu W, et al: Bioavailability of albumin-bound testosterone. *J Clin Endocrinol Metab.* 1985 Oct;61(4):705-10
2. New MI, Josso N: Disorders of gonadal differentiation and congenital adrenal hyperplasia. *Endocrinol Metab Clin North Am.* 1988 Jun;17(2):339-366
3. Morley JE, Perry HM III: Androgen deficiency in aging men: Role of testosterone replacement therapy. *J Lab Clin Med.* 2000 May;135(5):370-378
4. Sizonenko PC, Paunier L: Hormonal changes in puberty III: Correlation of plasma dehydroepiandrosterone, testosterone, FSH and LH with stages of puberty and bone age in normal boys and girls and in patients with Addison's disease or hypogonadism or with premature or late adrenarche. *J Clin Endocrinol Metab.* 1975 Nov;41(5):894-904
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7. Juul A, Skakkebaek NE: Androgens and the aging male. *Hum Reprod Update.* 2002 Sep-Oct;8(5):423-433
8. Hackbarth JS, Hoyne JB, Grebe SK, Singh RJ: Accuracy of calculated free testosterone differs between equations and depends on gender and SHBG concentration. *Steroids.* 2011 Jan;76(1-2):48-55
9. Goldman AL, Bhasin S, Wu FCW, et al: A reappraisal of testosterone's binding in circulation: Physiological and clinical implications. *Endocr Rev.* 2017 Aug;38(4):302-324

Performance**Method Description**

Deuterated stable isotope (d3-testosterone) is added to a 0.2 mL serum sample as internal standard. Protein is precipitated from the mixture by the addition of acetonitrile. The testosterone and internal standard are extracted from the resulting supernatant by an online extraction utilizing high-throughput liquid chromatography (HTLC). This is followed by conventional liquid chromatography and analysis on a tandem mass spectrometer equipped with a heated nebulizer ion source. (Wang C, Catlin DH, Demers LM, et al: Measurement of total testosterone in adult men: comparison of current laboratory methods versus liquid chromatography-tandem mass spectrometry. J Clin Endocrinol Metab. 2004;89:534-543; Taieb J, Mathian B, Millot F, et al: Testosterone measured by 10 immunoassays and by isotope-dilution gas chromatography-mass spectrometry in Sera from 116 men, women, and children. Clin Chem. 2003;49:1381-1395)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

2 to 3 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees & Codes**Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

84403

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TTST	Testosterone, Total, S	2986-8

Test Definition: TTST

Testosterone, Total, Mass Spectrometry,
Serum

Result ID	Test Result Name	Result LOINC® Value
8533	Testosterone, Total, S	2986-8