Overview

Useful For

Testosterone, Total:

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

-Evaluation of women with hirsutism, virilization, and oligo-amenorrhea

-Evaluation of women with symptoms or signs of possible testosterone deficiency

-Evaluation of infants with ambiguous genitalia or virilization

-Diagnosis of androgen-secreting tumors

Testosterone, Total and Bioavailable

-This is the recommended second-level test for suspected increases or decreases in physiologically active testosterone

-Assessment of androgen status in cases with suspected or known sex hormone-binding globulin binding abnormalities

-Assessment of functional circulating testosterone in early pubertal boys and older men

-Assessment of functional circulating testosterone in women with symptoms or signs of hyperandrogenism but normal total testosterone levels

-Monitoring of testosterone therapy or antiandrogen therapy in older men and in females

Profile Information

Test ID	Reporting Name	Available Separately	Always Performed
BATS	Testosterone, Bioavailable, S	No	Yes
TTST	Testosterone, Total, S	Yes	Yes

Method Name

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

BATS: Differential Precipitation

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Advisory Information

This is the first-level test for suspected increases or decreases in physiologically active testosterone.

Necessary Information

Patient's age and sex are required.

Specimen Required

Container/Tube: Red top

Specimen Volume: 1 mL

Specimen Minimum Volume

0.6 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK
Other	Serum Gel

Specimen Stability Information

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

Clinical and 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 also exerts anabolic effects and influences behavior.

In men, 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 adrenals

and peripheral tissues. After menopause, ovarian testosterone production is significantly diminished. Testosterone production in testes and ovaries is regulated via pituitary-gonadal feedback involving lutenizing hormone (LH), and to a lesser degree, inhibins and activins.

Most circulating testosterone is bound to sex hormone-binding globulin (SHBG), which in men also is called testosterone-binding globulin. A lesser fraction is albumin bound and a small proportion exists as free hormone. Historically, only the 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, oligo-amenorrhea, or infertility. Mild-to-moderate testosterone elevations are usually asymptomatic in males, but can cause distressing symptoms in females. The exact causes for mild-to-moderate elevations in testosterone often remain obscure. Common causes of pronounced elevations of testosterone 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 men, 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 (TTST / Testosterone, Total, Serum) is often sufficient for diagnosis, particularly if it is combined with measurements of LH (LH / Luteinizing Hormone [LH], Serum) and follicle stimulating hormone (FSH) (FSH / Follicle-Stimulating Hormone [FSH], Serum). However, these tests may be insufficient for diagnosis of mild abnormalities of testosterone homeostasis, particular 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. While both bioavailable and free testosterone can be used for the same indications, determination of bioavailable testosterone levels may be superior to free testosterone measurement in most situations.

Reference Values

TESTOSTERONE, TOTAL

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.

TESTOSTERONE, BIOAVAILABLE

Males

< or =19 years: not established

20-29 years: 83-257 ng/dL

30-39 years: 72-235 ng/dL

40-49 years: 61-213 ng/dL

50-59 years: 50-190 ng/dL

60-69 years: 40-168 ng/dL

> or =70 years: not established

Females (non-oophorectomized)

< or =19 years: not established

20-50 years (on oral estrogen): 0.8-4.0 ng/dL

20-50 years (not on oral estrogen): 0.8-10 ng/dL

>50 years: not established

Interpretation

Total Testosterone and general interpretation of testosterone abnormalities:

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's syndrome, XX 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 hypogonadotrophic hypogonadism, shows low testosterone and low, or inappropriately "normal," LH/FSH levels. Causes include:

-Inherited or developmental disorders of hypothalamus and pituitary (eg, Kallmann's syndrome, congenital hypopituitarism)

-Pituitary or hypothalamic tumors

-Hyperprolactinemia of any cause

-Malnutrition

-Excessive exercise

-Cranial irradiation

-Head trauma

-Medical or recreational drugs (eg, estrogens, GNRH analogs, cannabis)

Increased testosterone levels:

In prepubertal boys, increased levels of testosterone are seen in precocious puberty. Further work-up is necessary to determine the cause(s) of precocious puberty.

In adult men, 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).

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. Nonclassical (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 OH-progesterone (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 exceed 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.

Testosterone, Total and Bioavailable:

Usually, bioavailable (and free testosterone) levels parallel the total testosterone levels. However, a number of conditions and medications are known to increase or decrease the sex hormone-binding globulin (SHBG) concentration, which may cause total testosterone concentration to change without necessarily influencing the bioavailable or free testosterone concentration, or vice versa:

-Treatment with corticosteroids and sex steroids (particularly oral conjugated estrogen) can result in changes in SHBG levels and availability of sex-steroid binding sites on SHBG. This may make diagnosis of subtle testosterone abnormalities difficult.

-Inherited abnormalities in SHBG binding.

-Liver disease and severe systemic illness.

-In pubertal boys and adult men, mild decreases of total testosterone without LH abnormalities can be associated with delayed puberty or mild hypogonadism. In this case, either bioavailable or free testosterone measurements are better indicators of mild hypogonadism than determination of total testosterone levels.

-In polycystic ovarian syndrome and related conditions, there is often significant insulin resistance, which is associated with low SHBG levels.

-Consequently, bioavailable or free testosterone levels may be more significantly elevated.

Either bioavailable (TTBS / Testosterone, Total and Bioavailable, Serum) or free testosterone (TGRP / Testosterone, Total and Free, Serum) should be used as supplemental tests to total testosterone in the above situations. The correlation coefficient between bioavailable and free testosterone (by equilibrium dialysis) is 0.9606. However, bioavailable testosterone is usually the preferred test, as it more closely reflects total bioactive testosterone,

particularly in older men. These men not only have elevated SHBG levels, but albumin levels may also vary, due to coexisting illnesses.

Cautions

Early morning testosterone levels in young male individuals are on average 50% higher than p.m. levels. Our reference ranges have been derived from a.m. specimens.

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

The low end of the normal reference range in prepubertal subjects is not yet established.

Supportive Data

Correlates well with free testosterone by equilibrium dialysis (r=0.9606; n=199)

Clinical Reference

1. Manni A, Pardridge WM, Cefalu W, et al: Bioavailability of albumin-bound testosterone. J Clin Endocrinol Metab 1985;61:705

2. New MI, Josso N: Disorders of gonadal differentiation and congenital adrenal hyperplasia. Endocrinol Metab Clin North Am 1988;17:339-366

3. Dumesic DA: Hyperandrogenic anovulation: a new view of polycystic ovary syndrome. Postgrad Obstet Gynecol 1995 June;15(13)

4. Morley JE, Perry HM III: Androgen deficiency in aging men: Role of testosterone replacement therapy. J Lab Clin Med 2000;135:370-378

Performance

Method Description

Testosterone, Bioavailable:

The method is based on the differential precipitation of sex hormone-binding globulin (SHBG) by ammonium sulfate following equilibration of the serum specimen and tracer amounts of tritium-labeled testosterone. The results are expressed as the percent of testosterone free or albumin bound (not precipitated with SHBG) compared to an albumin standard. The product of this percentage and the total testosterone measurement is the total bioavailable testosterone.(Wheeler MJ: The determination of bio-available testosterone. Ann Clin Biochem 1995;32:345-357)

Testosterone, Total:

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) and Time(s) Test Performed

Monday through Friday

Analytic Time

Same day/1 day

Maximum Laboratory Time

4 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees and 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 U.S. Food and Drug Administration.

CPT Code Information

84403

84410

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
TTBS	Testosterone, Total and Bioavail, S	In Process

Result ID	Test Result Name	Result LOINC Value
82978	Testosterone, Bioavailable, S	2990-0
8533	Testosterone, Total, S	2986-8