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Testosterone

Aiding in the diagnosis of androgen dysfunction and hypogonadism

Testosterone is a steroid hormone that is commonly measured for various diagnostic purposes. Testosterone results can be used to evaluate hypogonadal men for primary or secondary testicular dysfunction. In men, low levels of testosterone are a possible cause of reduced fertility or lack of libido.[1–3] In women, testosterone results can be used to evaluate conditions of androgen excess, such as PCOS (polycystic ovarian syndrome), hirsutism, suspected androgen-producing neoplasm, and conditions that may affect fertility, such as anovulation or amenorrhea with virilization.[4,5] Testosterone measurement may also be helpful in menopausal women with suspected testosterone deficiency.[5] Testosterone results in children can be used to aid in the diagnosis and treatment of premature puberty, genetic diseases — such as congenital adrenal hyperplasia — and over-virilization or under-virilization at birth.[4]

Recent research suggests that maintaining the appropriate levels of testosterone may benefit men with osteoporosis, type 2 diabetes, cardiovascular disease, obesity, and depression.[1,2] Androgen replacement therapy in postmenopausal women has also been studied as a means of boosting bone density and muscle mass.[6] The recent epidemic of obesity in children has led to an increase in the assessment of androgen status in these patients because obesity has been associated with precocious puberty.[6]

Commonly used methods for testosterone measurements in the clinical laboratory include direct immunoassays (RIA, ELISA, ICMA, EIA, ECLIA, etc), immunoassays after extraction and chromatography, and (more recently) mass spectrometry methods. Each method offers unique strengths and shortcomings, and the choice of methods depends on the physician's intended use and the performing laboratory's technical expertise.[7]

Testosterone Testing Recommendations

Historically, testosterone levels were primarily used in the work-up of men suspected of hypogonadism and in gender assignment for newborns with ambiguous genitalia.[4] The Endocrine Society and the American Society for Andrology recommend using the total testosterone measurement, preferably obtained on more than one morning sample — as a screening test for hypogonadism in men — and concluded that most direct immunoassays distinguish between testosterone concentrations found in classic hypogonadism and normal levels.[7,8] Monitoring hypogonadal males during testosterone replacement therapy, however, requires more sensitive and accurate assays.[7]

Due to its expanded clinical applications, measurement of testosterone levels in women and children has increased in recent years.[6] Its most common application in women is as an aid in the diagnosis of hyperandrogenic states. It is reported that most direct immunoassays are adequate for identifying, but not accurately quantifying, elevated testosterone in women.[7]

The Endocrine Society recommends that testosterone determination in children be performed using assays with sufficient sensitivity and in conjunction with appropriate reference intervals.[7] Populations with low testosterone concentrations, such as women, children, and hypogonadal males, require more attention to the assay's analytical sensitivity and specificity. One of the methods that may offer an appropriate level of sensitivity and specificity for these populations is high-pressure liquid chromatography and tandem mass spectrometry (HPLC/MS-MS).[7]

Testosterone Assay Standardization

Another concern regarding laboratory measurements of testosterone is the lack of standardization among methodologies.[9] In early 2010, a group of professional associations, government agencies, and commercial entities met to discuss issues regarding testosterone assay standardization, including a consensus effort regarding the need for accurate testosterone testing. The consensus effort is being led by the Centers for Disease Control and Prevention (CDC).[6] In addition to LabCorp, organizations endorsing the consensus effort for accurate testosterone testing include[10,11]

- American Association for Clinical Chemistry
- American Association of Clinical Endocrinologists
- American Society for Bone and Mineral Research
- American Society for Reproductive Medicine
- American Urological Association
- Androgen Excess and PCOS Society
- Association of Public Health Laboratories
- North American Menopause Society
- Pediatric Endocrine Society
- The Endocrine Society

The new CDC Hormone Standardization (HoSt) program issues certificates annually to laboratories that demonstrate performance within the established criteria, enabling harmonization of testosterone test results across laboratories and methodologies.[6,11,12]

LabCorp Testosterone Test Options

LabCorp offers a comprehensive menu of testosterone methods to meet the testing needs for various patient conditions. In addition to a next-generation direct immunoassay from Roche (ECLIA), LabCorp also offers a highly sensitive and specific high-pressure liquid chromatography and tandem mass spectrometry (LC/MS-MS) method. The LC/MS-MS method is currently certified by the CDC HoSt program.

The direct ECLIA testosterone immunoassay (004226) is appropriate for use as an aid in screening for androgen dysfunctions in adult males. It is sufficiently sensitive and accurate for this purpose and allows fast turnaround time for test results.[7]

The LC/MS-MS assay (070001) can aid in the diagnosis of androgen dysfunction in females and children as well as for monitoring male patients diagnosed with hypogonadism. It is a more sensitive and specific method when measuring very low testosterone concentrations when compared to immunoassay.[7]

References

1. Kaufman JM, Vermeulen A. The decline of androgen levels in elderly men and its clinical and therapeutic implications. *Endocr Rev*. 2005 Oct; 26(6):833–876.
2. Stanworth RD, Jones TH. Testosterone for the aging male; current evidence and recommended practice. *Clin Interv Aging*. 2008 Jan; 3(1):25–44.
3. Bhasin S, Cunningham GR, et al. Testosterone therapy in men with androgen deficiency syndromes: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2010 Jun; 95(6):2536–2559.
4. 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 Aug; 49(8):1381–1395.
5. Casson PR, Toth MJ, Johnson JV, Stanczyk FZ, Casey CL, Dixon ME. Correlation of serum androgens with anthropometric and metabolic indices in healthy, nonobese postmenopausal women. *J Clin Endocrinol Metab*. 2010 Sep; 95(9):4276–4282.
6. Rollins G. The trials of testosterone testing: Immunoassays faulty in women and children, but what's the solution? *Clinical Laboratory News*. 2010 Aug; 36(8):1,4–5.
7. Rosner W, Auchus RJ, Azziz R, et al. Utility, limitations, and pitfalls in measuring testosterone: An Endocrine Society position statement. *J Clin Endocrinol Metab*. 2007 Feb; 92(2):405–413. PubMed 17090633.
8. Wang C, Nieshlag E, Swerdloff R, et al. Investigation, treatment, and monitoring of late-onset hypogonadism in males: ISA, ISSAM, EAU, EAA and ASA recommendations. *J Androl*. 2009 Jan-Feb; 30(1):1–9.
9. Thienpont LM, Van Uytfanghe K, Blincko S, et al. State-of-the-art of serum testosterone measurement by isotope dilution-liquid chromatography-tandem mass spectrometry. *Clin Chem*. 2008 Aug; 54(8):1290–1297. PubMed 18556330
10. Doan LL. Moving toward excellence in testosterone testing. *Endocrine News*. 2010 Apr: 25.
11. Rosner W, Vesper H; Endocrine Society, et al. Toward excellence in testosterone testing: A consensus statement. *J Clin Endocrinol Metab*. 2010 Oct; 95(10):4542–4548.
12. Vesper HW, Botelho JC. *CDC-Hormone Standardization Project (CDC-HoSt Project): Standardization of Serum Total Testosterone Measurements.* Atlanta, Ga: CDC.

Testosterone, Total, Women, Children, and Hypogonadal Males, LC/MS-MS 070001

Special Instructions State the patient's age and sex on the test request form.

Specimen Serum

Volume 0.8 mL

Minimum Volume 0.4 mL (**Note:** This volume does not allow for repeat testing.)

Container Red-top tube or gel-barrier tube

Collection If a red-top tube is used, transfer separated serum to a plastic transport tube.

Storage Instructions Refrigerate.

Reference Interval See table to the right.

Premature Infants	Males (ng/dL)	Females (ng/dL)
26 – 28 Weeks, Day 4	59.0 – 125.0	5.0 – 16.0
31 – 35 Weeks, Day 4	37.0 – 198.0	5.0 – 22.0
Full-term Infants		
Newborn	75.0 – 400.0	20.0 – 64.0
1 – 7 Months	Levels decrease rapidly the first week to 20.0 – 50.0 ng/dL, then increase to 60.0 – 400.0 ng/dL (Mean = 190) between 20 – 60 days. Levels then decline to prepubertal range of <2.5 – 10.0 by seven months.	Levels decrease during the first month to <10.0 ng/dL and remain there until puberty.
Prepubertal Children		
1 – 10 Years	< 2.5 – 10.0	NA
1 – 9 Years	NA	< 2.5 – 10.0

Puberty

Tanner Stage	Age (Years)	Range (ng/dL)	Mean (ng/dL)
Male			
1	< 9.8	< 2.5 – 10.0	4.9
2	9.8 – 14.5	18.0 – 150.0	42.0
3	10.7 – 15.4	100.0 – 320.0	190.0
4	11.8 – 16.2	200.0 – 620.0	372.0
5	12.8 – 17.3	350.0 – 970.0	546.0
Female			
1	<9.2	< 2.5 – 10.0	4.9
2	9.2 – 13.7	7.0 – 28.0	18.0
3	10.0 – 14.4	15.0 – 35.0	25.0
4	10.7 – 15.6	13.0 – 32.0	22.0
5	11.8 – 18.6	20.0 – 38.0	28.0

Adults		
≥18 Years	348.0 – 1197.0	NA
Premenopausal	NA	10.0 – 55.0
Postmenopausal	NA	7.0 – 40.0

Use This assay provides the sensitivity and specificity required for the assessment of the low testosterone levels found in women, children, adolescents, and hypogonadal men.[7]

Limitations Drugs, including androgens and steroids, can decrease testosterone levels. Men with advanced prostate cancer often receive drugs that lower testosterone levels. Women receiving estrogen may have increased testosterone levels. Anticonvulsants, barbiturates, and clomiphene can cause testosterone levels to rise.

Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at **www.LabCorp.com**.

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