MAYO CLINIC LABORATORIES

Test Definition: ANST

Androstenedione, Serum

Overview

Useful For

Diagnosis and differential diagnosis of hyperandrogenism, in conjunction with measurements of other sex steroids

Diagnosis of congenital adrenal hyperplasia (CAH), in conjunction with measurement of other androgenic precursors, particularly, 17-alpha-hydroxyprogesterone (OHPG), 17 alpha-hydroxypregnenolone, dehydroepiandrosterone sulfate (DHEA-S), and cortisol

Monitoring CAH treatment, in conjunction with testosterone, OHPG, DHEA-S, and DHEA

Diagnosis of premature adrenarche, in conjunction with measurement of follicle-stimulating hormone and luteinizing hormone as well as other adrenal and gonadal sex-steroids and their precursors

Testing Algorithm

For more information see Steroid Pathways.

Special Instructions

- Steroid Pathways

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Additional Testing Requirements

For diagnosis and differential diagnosis of hyperandrogenism, an initial workup in adults should also include total and bioavailable testosterone (TTBS / Testosterone, Total and Bioavailable, Serum) measurements. Depending on results, this may be supplemented with measurements of sex hormone-binding globulin (SHBG1 / Sex Hormone-Binding Globulin, Serum) and other androgenic steroids (eg, dehydroepiandrosterone sulfate [DHEA-S]).

For diagnosis of congenital adrenal hyperplasia (CAH), the following assays should also be ordered:
-OHPG / 17-Hydroxyprogesterone, Serum
-DHES1 / Dehydroepiandrosterone Sulfate, Serum
-CORT / Cortisol, Serum

For monitoring CAH treatment, the following assays should also be ordered:
-TTST / Testosterone, Total, Mass Spectrometry, Serum
-OHPG / 17-Hydroxyprogesterone, Serum
-DHES1 / Dehydroepiandrosterone Sulfate, Serum
-DHEA_ / Dehydroepiandrosterone [DHEA], Serum.

For diagnosis of premature adrenarche, the following assays should also be ordered:
-FSH / Follicle-Stimulating Hormone [FSH], Serum
-LH / Luteinizing Hormone [LH], Serum
-TTBS / Testosterone, Total and Bioavailable, Serum or TGRP / Testosterone, Total and Free, Serum
-EEST / Estradiol, Serum
-DHES1 / Dehydroepiandrosterone Sulfate, Serum
-DHEA_ / Dehydroepiandrosterone (DHEA), Serum
-SHBG1 / Sex Hormone-Binding Globulin, Serum
-OHPG / 17-Hydroxyprogesterone, Serum

Specimen Required

Collection Container/Tube: Red top (serum gel/SST are **not acceptable)**
Submission Container/Tube: Plastic vial
Specimen Volume: 0.6 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial

Specimen Minimum Volume

0.25 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	28 days	
	Ambient	7 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Androstenedione is secreted predominately by the adrenal gland and production is at least partly controlled by

adrenocorticotropic hormone (ACTH). It is also produced independent of ACTH in the testes and ovaries from adrenal-secreted dehydroepiandrosterone sulfate (DHEA-S). Androstenedione is a crucial sex-steroid precursor. It lies at the convergence of the 2 biosynthetic pathways that lead from the progestins to the sex steroids, being derived either via:
-C3-dehydrogenation of DHEA
-Catalyzed by 3-beta-hydroxysteroid dehydrogenase-2 (adrenals and gonads)
-17,20-lyase (*CYP17A1*)-mediated side-chain cleavage of 17-alpha-hydroxyprogesterone (OHPG)

Androstenedione production during life mimics the pattern of other androgen precursors. Fetal serum concentrations increase throughout embryonal development and peak near birth at approximately young adult levels. Levels then fall rapidly during the first year of life to low prepubertal values. With the onset of adrenarche, androstenedione rises gradually, a process that accelerates with the onset of puberty, reaching adult levels around age 18. Adrenarche is a poorly understood phenomenon peculiar to higher primates that is characterized by a gradual rise in adrenal androgen production. It precedes puberty but is not causally linked to it. Early adrenarche is not associated with early puberty, or with any reduction in final height, or overt androgenization, and is generally regarded as a benign condition not requiring intervention. However, girls with early adrenarche may be at increased risk of polycystic ovarian syndrome as adults, and some boys may develop early penile enlargement.

Elevated androstenedione levels can cause symptoms or signs of hyperandrogenism in women. Men are usually asymptomatic but through peripheral conversion of androgens to estrogens, can occasionally experience mild symptoms of estrogen excess, such as gynecomastia.

Most mild-to-moderate elevations in androstenedione are idiopathic. However, pronounced elevations of androstenedione may be indicative of androgen-producing adrenal or gonadal tumors.

In children, adrenal and gonadal tumors are uncommon, but many forms of congenital adrenal hyperplasia can increase serum androstenedione concentrations. Diagnosis always requires measurement of other androgen precursors (eg, OHPG, 17-alpha-hydroxypregnenolone, and DHEA-S) and cortisol, in addition to androstenedione.

For more information see Steroid Pathways.

Reference Values

PEDIATRICS*

Infants	Age	Reference range (ng/dL)
Premature: 26-28 weeks	4 days	92-282 ng/dL
Premature: 31-35 weeks	4 days	80-446 ng/dL
Full term	1-7 days	20-290 ng/dL
Full term	1 month-1 year	<69 ng/dL

*Male Tanner stages	Age (Years)	Reference range (ng/dL)
Stage I (prepubertal)	<9.8	<51
Stage II	9.8-14.5	31-65
Stage III	10.7-15.4	50-100
Stage IV	11.8-16.2	48-140

Stage V	12.8-17.3	65-210

*Female Tanner stages	Age (Years)	Reference range (ng/dL)
Stage I (prepubertal)	<9.2	<51
Stage II	9.2-13.7	42-100
Stage III	10.0-14.4	80-190
Stage IV	10.7-15.6	77-225
Stage V	11.8-18.6	80-240

*Soldin SJ, Brugnara C, Wong EC, eds. Androstenedione. In: Pediatric Reference Ranges. 4th ed. AACC Press; 2003: 32-34

ADULTS
Males: 40-150 ng/dL
Females: 30-200 ng/dL

For SI unit Reference Values, see www.mayocliniclabs.com/order-tests/si-unit-conversion.html

Interpretation

Elevated androstenedione levels indicate increased adrenal or gonadal androgen production. Mild elevations in adults are usually idiopathic or related to conditions, such as polycystic ovarian syndrome (PCOS) in women or use of androstenedione supplements in men and women. However, levels greater than or equal to 500 ng/dL can suggest the presence of an androgen-secreting adrenal or, less commonly, a gonadal tumor. Androstenedione levels are elevated in more than 90% of patients with benign androgen-producing adrenal tumors, usually well above 500 ng/dL. Most androgen-secreting adrenal carcinomas also exhibit elevated androstenedione levels but more typically show relatively larger elevations in 17-alpha-hydroxyprogesterone (OHPG) and dehydroepiandrosterone sulfate (DHEA-S) than in androstenedione, as they have often lost the ability to produce downstream androgens.

Most androgen-secreting gonadal tumors overproduce androstenedione, often to lesser degrees than adrenal tumors. They also overproduce testosterone. In men and in women with high baseline androgen levels (eg, PCOS), the respective elevations of androstenedione and testosterone may not be high enough to allow unequivocal diagnosis of androgen-producing gonadal tumors. In these cases, an elevation of the usual ratio of testosterone to androstenedione of 1, to a ratio of greater than 1.5, is a strong indicator of neoplastic androgen production.

Diagnosis and differential diagnosis of congenital adrenal hyperplasia (CAH) always requires the measurement of several steroids. Patients with CAH due to 21-hydroxylase gene (*CYP21A2*) variants, the most common cause of CAH (>90% of cases), usually have very high levels of androstenedione, often 5- to 10-fold elevations. OHPG levels are usually even higher, while cortisol levels are low or undetectable. All 3 analytes should be tested.

In the much less common *CYP11A1* variant, androstenedione levels are elevated to a similar extent as in the *CYP21A2* variant, and cortisol is also low, but OHPG is only mildly, if at all, elevated.

Also less common, 3-beta hydroxysteroid dehydrogenase (HSD) type 2 deficiency is characterized by low cortisol and substantial elevations in DHEA-S and 17-alpha hydroxypregnenolone, while androstenedione is either low, normal, or, rarely, very mildly elevated (as a consequence of peripheral tissue androstenedione production by 3-beta HSD-1).

In the very rare STAR (steroidogenic acute regulatory protein) deficiency, all steroid hormone levels are low, and cholesterol is elevated.

In the also very rare 17-alpha-hydroxylase deficiency, androstenedione, all other androgen-precursors (17-alpha-hydroxypregnenolone, OHPG, DHEA-S), androgens (testosterone, estrone, estradiol), and cortisol are low, while production of mineral corticoid and their precursors, in particular progesterone, 11-deoxycorticosterone, corticosterone, and 18-hydroxycorticosterone, are increased.

The goal of CAH treatment is normalization of cortisol levels and, ideally, also of sex-steroid levels. Traditionally, OHPG and urinary pregnanetriol or total ketosteroid excretion are measured to guide treatment, but these tests correlate only modestly with androgen levels. Therefore, androstenedione and testosterone should also be measured and used for treatment modifications. Normal prepubertal levels may be difficult to achieve, but if testosterone levels are within the reference range, androstenedione levels up to 100 ng/dL are usually regarded as acceptable.

Girls younger than 7 to 8 years of age and boys younger than 8 to 9 years of age who present with early development of pubic hair or, in boys, penile enlargement, may be suffering from either premature adrenarche or premature puberty, or both. Measurement of DHEA-S, DHEA, and androstenedione, alongside determination of sensitive estradiol, total and bioavailable or free testosterone, sex hormone binding globulin (SHBG), and luteinizing hormone/follicle-stimulating hormone levels will allow correct diagnosis in most cases. In premature adrenarche, only the adrenal androgens, chiefly DHEA-S, and to a lesser degree, androstenedione, will be above prepubertal levels, whereas early puberty will also show a fall in SHBG levels and variable elevations of gonadotropins and gonadal sex-steroids above the prepuberty reference range.

For more information see Steroid Pathways.

Cautions

Any condition that can result in partial or complete adrenal or gonadal failure may result in low androstenedione levels, diminishing the diagnostic usefulness of the test in these settings.

Androstenedione and, to a lesser degree, dehydroepiandrosterone sulfate (DHEA-S) supplements can result in elevations of serum androstenedione level. With large androstenedione doses of 300 to 400 mg/day, serum androstenedione levels can almost double in some patients. Testosterone levels and, particularly in men, estrone and estradiol levels, may also increase but to a much lesser degree.

Although compared with DHEA-S, less information has been published with regard to the effects of hormones and drugs on androstenedione levels, it is likely that many drugs and hormones can result in changes in androstenedione levels. In particular, agents that induce hepatic enzymes, drugs that affect lipid metabolism, and other steroid hormones are likely to affect androstenedione levels, more commonly resulting in lowered levels. Whether any of these secondary changes are of clinical significance and how they should be related to the established normal reference ranges is unknown. In most cases, the drug-induced changes are not large enough to cause diagnostic confusion.

Supportive Data

To establish pediatric reference ranges, we compared adult levels obtained with our liquid chromatography tandem mass spectrometry methodology with adult levels obtained in other labs with their respective methodologies. We found excellent correlation (R=0.92, regression-trendline slope 1.07) with an extracted radioimmunoassay (RIA) method with

preanalytical Sephradex column chromatography. This is the method used in Pediatric Reference Ranges, 4th edition and is based on reference 1. The ranges were further verified by comparison with another pediatric reference range publication, which used the same extracted RIA method with Sephradex column chromatography.(2)

Clinical Reference

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Performance

Method Description
Deuterated stable isotopes (d4-cortisol, d7-androstenedione, d8 17-hydroxyprogesterone) are added to the serum sample as internal standards. Cortisol, androstenedione, 17-hydroxyprogesterone, and the internal standards are extracted from specimens online using a guard cartridge. The analytes are transferred online to an analytical column and are analyzed by liquid chromatography tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
2 to 5 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
82157

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ANST	Androstenedione, S	1854-9

Result ID	Test Result Name	Result LOINC® Value

7730	Androstenedione, S	1854-9