MAYO CLINIC LABORATORIES

Test Definition: CAH21

Congenital Adrenal Hyperplasia (CAH) Profile
for 21-Hydroxylase Deficiency, Serum

Overview

Useful For

Preferred screening test for congenital adrenal hyperplasia (CAH) caused by 21-hydroxylase deficiency

Part of a battery of tests to evaluate women with hirsutism or infertility, which can result from adult-onset CAH

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
CORTI	Cortisol, S	Yes, (order CINP)	Yes
ANDRO	Androstenedione, S	Yes, (order ANST)	Yes
H17	17-Hydroxyprogesterone, S	Yes, (order OHPG)	Yes

Genetics Test Information

This is the preferred screening test for congenital adrenal hyperplasia (CAH) caused by 21-hydroxylase deficiency. It is also useful as part of a battery of tests to evaluate female individuals with hirsutism or infertility, which can result from adult-onset CAH.

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

Ordering Guidance

This profile provides the simultaneous determination of 17-hydroxyprogesterone, androstenedione, and cortisol. These steroids can also be ordered individually: OHPG / 17-Hydroxyprogesterone, Serum; ANST / Androstenedione, Serum; and CINP / Cortisol, Mass Spectrometry, Serum.

Specimen Required

Collection Container/Tube: Red top (serum gel/SST are **not acceptable**)
Submission Container/Tube: Plastic vial
Specimen Volume: 0.6 mL Serum

Collection Instructions:
1. Morning (8 a.m.) and afternoon (4 p.m.) specimens are preferred.
2. Include time of collection.
3. Centrifuge and aliquot serum into a plastic vial.

Additional Information: If multiple specimens are collected, send a separate order for each specimen.

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

Serum: 0.25 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	14 days	
	Ambient	7 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Congenital adrenal hyperplasia (CAH) is caused by an inherited genetic defect that results in decreased formation of one of the many enzymes required for cortisol synthesis. The enzyme defect results in decreased glucocorticoid and mineralocorticoid production and increased 17-hydroxyprogesterone (OHPG) and androgen concentrations. The resulting hormone imbalances can lead to life-threatening, salt-wasting crises in newborns and incorrect sex assignment of virilized female infants. Adult-onset CAH may cause hirsutism or infertility in women.

17-Hydroxyprogesterone is produced by the adrenal glands, ovaries, testes, and placenta. It is hydroxylated at the 11 and 21 positions to produce cortisol. Deficiency of either 11- or 21-hydroxylase decreases cortisol synthesis and disrupts feedback inhibition of adrenocorticotropic hormone (ACTH) secretion. Consequently, increased pituitary release of ACTH increases production of OHPG. In contrast, if 17-alpha-hydroxylase, which is required to form OHPG from progesterone, or 3-beta-hydroxysteriod dehydrogenase, which is required to form OHPG from 17-hydroxypregnenolone, are deficient, OHPG concentrations are low with possible increases in progesterone or pregnenolone, respectively.

Most (90%) cases of CAH are caused by genetic variants in the 21-hydroxylase gene (*CYP21A2*). CAH due to

21-hydroxylase deficiency is diagnosed by confirming elevations of OHPG and androstenedione concentrations with decreased cortisol concentration. By contrast, in the less common forms of CAH caused by 17-hydroxylase or 11-hydroxylase deficiency, OHPG and androstenedione concentrations are not significantly increased. Measurement of progesterone (PGSN / Progesterone, Serum) or deoxycorticosterone (DOCS / 11-Deoxycorticosterone, Serum), respectively, is necessary for diagnosis.

17-Hydroxyprogesterone binds to both transcortin and albumin. Total OHPG is measured in this assay. OHPG is metabolized to pregnanetriol, which is conjugated and excreted in the urine. More specific tests than pregnanetriol measurement are available for diagnosing disorders of steroid metabolism.

Reference Values

CORTISOL
5-25 mcg/dL (a.m.)
2-14 mcg/dL (p.m.)
Pediatric reference values are the same as adults, as confirmed by peer-reviewed literature.
Petersen KE. ACTH in normal children and children with pituitary and adrenal diseases. I. Measurement in plasma by radioimmunoassay-basal values. Acta Paediatr Scand. 1981;70(3):341-345

ANDROSTENEDIONE
Pediatrics*
Premature infants
26-28 weeks, day 4: 92-282 ng/dL
31-35 weeks, day 4: 80-446 ng/dL
Full-term infants
1-7 days: 20-290 ng/dL
1 month-1 year: <69 ng/dL

Males*

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

Females*

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. Androstenedione. In: Pediatric Reference Ranges. 4th ed. AACC Press; 2003:32-34

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

17-HYDROXYPROGESTERONE
Children
Preterm infants: Preterm infants may exceed 630 ng/dL, however, it is uncommon to see levels reach 1,000 ng/dL.
Term infants
0-28 days: <630 ng/dL
Levels fall from newborn (<630 ng/dL) to prepubertal gradually within 6 months.
Prepubertal males: <110 ng/dL
Prepubertal females: <100 ng/dL

Adults
Males: <220 ng/dL
Females
Follicular: <80 ng/dL
Luteal: <285 ng/dL
Postmenopausal: <51 ng/dL

Note: For pregnancy reference values, see: Soldin OP, Guo T, Weiderpass E, Tractenberg RE, Hilakivi-Clarke L, Soldin SJ. Steroid hormone levels in pregnancy and 1 year postpartum using isotope dilution tandem mass spectrometry. Fertil Steril. 2005;84(3):701-710

Interpretation

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 usually have very high levels of androstenedione, often 5- to 10-fold elevations. 17-Hydroxyprogesterone (OHPG) levels are usually even higher, while cortisol levels are low or undetectable. All 3 analytes should be tested.

In the much less common *CYP11A* variant, androstenedione levels are elevated to a similar extent as in *CYP21A2* variant, and cortisol is also low, but OHPG is only mildly, if at all, elevated.

Also less common is 3-beta hydroxysteroid dehydrogenase (HSD) type 2 deficiency, characterized by low cortisol and substantial elevations in dehydroepiandrosterone sulfate (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 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 its precursors, in particular progesterone, 11-deoxycorticosterone, corticosterone, and 18-hydroxycorticosterone, are increased.

The goal of CAH treatment is normalization of cortisol levels and, ideally, of sex-steroid levels also. OHPG is measured to guide treatment, but this test correlates only modestly with androgen levels. Therefore, androstenedione and testosterone should also be measured and used to guide treatment modifications. Normal prepubertal levels may be difficult to achieve, but if testosterone levels are within the reference intervals, androstenedione levels up to 100 ng/dL are usually regarded as acceptable.

Cautions

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

This test provides merely supplementary information and should, therefore, never be employed as the sole diagnostic tool.

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
See Individual Unit Codes

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
82533
83498

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CAH21	CAH 21-Hydroxylase Profile	79221-8

Result ID	Test Result Name	Result LOINC® Value
30041	Androstenedione, S	1854-9
30042	17-Hydroxyprogesterone, S	1668-3
30040	Cortisol, S	2143-6
30070	AM Cortisol	9813-7
30071	PM Cortisol	9812-9