

Overview

Useful For

Screening test for congenital adrenal hyperplasia (CAH), caused by either 11- or 21-hydroxylase deficiency, when used in combination with testing for cortisol and androstenedione

As part of a battery of tests to evaluate women with hirsutism or infertility

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

Ordering Guidance

The preferred screening test for congenital adrenal hyperplasia caused by 21-hydroxylase deficiency is CAH21 / Congenital Adrenal Hyperplasia (CAH) Profile for 21-Hydroxylase Deficiency, Serum, which allows the simultaneous determination of 17-hydroxyprogesterone, androstenedione, and cortisol.

Necessary Information

Patient's age and sex are required.

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 plastic vial.

Forms

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

Specimen Minimum Volume

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)	28 days	
	Ambient	7 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Congenital adrenal hyperplasia (CAH) is caused by inherited defects in steroid biosynthesis. The resulting hormone imbalances with reduced glucocorticoids and mineralocorticoids and elevated 17-hydroxyprogesterone (OHPG) and androgens can lead to life-threatening, salt-wasting crisis in the newborn period and incorrect gender assignment of virtualized female patients. Adult-onset CAH may result in hirsutism or infertility in women.

The adrenal glands, ovaries, testes, and placenta produce OHPG. It is hydroxylated at the 11 and 21 position to produce cortisol. Deficiency of either 11- or 21-hydroxylase results in decreased cortisol synthesis, and feedback inhibition of adrenocorticotrophic hormone (ACTH) secretion is lost. Consequent increased pituitary release of ACTH increases production of OHPG. But, if 17-alpha-hydroxylase (which allows formation of OHPG from progesterone) or 3-beta-hydroxysteroid dehydrogenase type 2 (which allows formation of 17-hydroxyprogesterone formation from 17-hydroxypregnenolone) are deficient, OHPG levels are low with possible increase in progesterone or pregnenolone respectively.

OHPG is bound to both corticosteroid binding globulin and albumin, and total OHPG is measured in this assay. OHPG is converted to pregnanetriol, which is conjugated and excreted in the urine. In all instances, more specific tests are available to diagnose disorders or steroid metabolism than pregnanetriol measurement.

Most (90%) cases of CAH are due to variants in the steroid 21-hydroxylase gene (*CYP21A2*). CAH due to 21-hydroxylase deficiency is diagnosed by confirming elevations of OHPG and androstenedione (ANST / Androstenedione, Serum) with decreased cortisol (CINP / Cortisol, Mass Spectrometry, Serum). By contrast, in 2 less common forms of CAH, due to 17-hydroxylase or 11-hydroxylase deficiency, OHPG and androstenedione levels are not significantly elevated and measurement of progesterone (PGSN / Progesterone, Serum) and deoxycorticosterone (DOCS / 11-Deoxycorticosterone, Serum), respectively, are necessary for diagnosis.

For more information see [Steroid Pathways](#)

Reference Values

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 ranges, see: Soldin OP, Guo T, Weiderpass E, et al. 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 steroid 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 *CYP11A1* 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.

In the also very rare 17-alpha-hydroxylase deficiency, androstenedione, all other androgen-precursors (17-alpha-hydroxypregnenolone, OHPG, dehydroepiandrosterone sulfate), androgens (testosterone, estrone, estradiol), and cortisol are low, while production of mineral corticoid and its precursors, in particular progesterone, 11-deoxycorticosterone, 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 to guide treatment modifications. Normal prepubertal levels may be difficult to achieve, but if testosterone levels are within the reference range, androstenedione levels of up to 100 ng/dL are usually regarded as acceptable.

For more information see [Steroid Pathways](#) .

Cautions

At birth the hypothalamic-pituitary-adrenal axis and the hypothalamic-pituitary-gonadal axis are activated, and adrenal

and sex steroid levels are high. In preterm infants, the elevations can be even more pronounced due to illness and stress. As a result, preterm infants may occasionally have 17-hydroxyprogesterone levels of up to 1000 ng/dL. Term infants (0-28 days) will have levels less than 630 ng/dL. These then fall over the following 1 to 6 months to prepubertal levels of less than 110 ng/dL (males) and less than 100 ng/dL (female patients).

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

83498

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
OHPG	17-Hydroxyprogesterone, S	1668-3

Result ID	Test Result Name	Result LOINC® Value
9231	17-Hydroxyprogesterone, S	1668-3