

Adrenal Steroids Panel

HIGH SPECIFICITY LC-MS/MS TEST FOR 11-DEOXYCORTISOL, 17-HYDROXYPROGESTERONE, 17-HYDROXYPREGNENOLONE, AND PREGNENOLONE IN SERUM

Test Highlights

This panel consists of four tests used to detect enzyme deficiencies that result in congenital adrenal hyperplasia (CAH). These four tests include 17-hydroxyprogesterone (17-OHP), 17-hydroxypregnenolone (17-OHPr), pregnenolone (Pr), and 11-deoxycortisol (11-DC).

Disease Overview

- CAH is a family of autosomal recessive disorders that occur due to a deficiency in one of the enzymes involved in cortisol synthesis (see figure 2, next page).
- The symptoms of the disorder depend upon which steroids are overproduced and which are deficient. As a result, CAH may present with various symptoms, including virilization of the affected female infant, signs of androgen excess in males and females, signs of sex hormone deficiency in males and females, salt-wasting crisis secondary to cortisol and aldosterone deficiency, or hormonal hypertension due to increased mineralocorticoids.
- The most common and the most studied of the enzymatic disorders is 21-hydroxylase deficiency, which results in the accumulation of 17-hydroxyprogesterone and diminished biosynthesis of cortisol.
- Patients with the severe form of CAH may have aldosterone and cortisol deficiency, resulting in a salt-wasting crisis in the newborn period between one week and one month of age. Diagnosis and treatment of affected infants in the neonatal period is necessary to minimize the morbidity and mortality associated with adrenal insufficiency. The diagnosis is usually accomplished by measuring blood levels of steroids of the cortisol synthesis pathway.
- A milder, non-classic form of CAH is characterized by premature puberty, acne, hirsutism, menstrual irregularity, and infertility.

Epidemiology

- Worldwide frequency of CAH is approximately one in 15,000 newborns, with increased frequency among certain ethnic groups (e.g., Eskimos, La Réunion in France).
- In Caucasians, the severe form of CAH is detected in one in 10,000 individuals, and the mild form is observed in one in 1,000.
- A milder, non-classic form of 21-hydroxylase occurs in Ashkenazi Jews, with estimated frequency of 0.1 percent. Approximately 90 percent of all cases of CAH are caused by 21-hydroxylase deficiency, while 5–8 percent are caused by 11 β -hydroxylase deficiency; 3 β -hydroxysteroid dehydrogenase and the other enzyme deficiencies are less common and account for 5–8 percent of all cases.

Genetics

When analyzing approximately 20 common mutations on chromosome 6p, it is possible to detect more than 90 percent of all

related defects. The remaining 10 percent of mutations are rare and can only be detected with direct sequencing of the entire *CYP21* gene.

Pathophysiology

Depending on the specific enzyme deficiency, CAH synthesis of some steroids may be blocked. This blockage leads to a decreased concentration of some of the steroids and the overproduction of the other steroids involved in the pathway (see figure 2, next page).

Indications for Ordering

- The 17-hydroxyprogesterone (17-OHP) test should be used in patients with the following symptoms:
 - Salt-wasting crisis
 - Males and females with pseudohermaphroditism
 - Postnatal virilization
 - Hirsutism
 - Infertility
 - Precocious pubarche
 - Disordered puberty
 - Menstrual irregularity
 - Acne
 - Hypertension
- This test should be used to monitor patients previously diagnosed with CAH.

Additional Ordering Notes

- In patients suspected of CAH, testing for a panel of steroids involved in the cortisol biosynthesis pathway (see figure 2, next page) should be performed in order to establish the specific enzyme deficiency.
- Please indicate the age and sex of the patient on the test request form and the test tube.

Interpretation

- In most cases, basal concentrations within the normal reference interval rule out CAH.
- Concentrations above the reference interval are suggestive of non-classic CAH, which can be confirmed with an ACTH stimulation test.
- The ratio of the precursor to the pathway product (with and without ACTH stimulation) may be used to diagnose which enzyme is deficient.

- False-negative results can occur due to circadian decrease in ACTH and during the follicular phase of the menstrual cycle due to increased production of 17-OHP.
- In figure 2 (next page), basal and post-ACTH 17-hydroxyprogesterone concentrations are compared with those of normal subjects for diagnosis of 21-hydroxylase deficiency.

Limitation

In some cases, definitive neonatal diagnosis is complicated by non-elevated 17-OHP levels in infants with 21-hydroxylase deficiency or by the presence of residual maternal-placental and fetal-steroid products.

Methodology

17-OHP, 17-OHPr, Pr, and 11-DC are extracted from the sample, derivatized, and analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The high specificity of LC-MS/MS is enhanced by the measurement of two product ions for each steroid, which allows for a qualitative assessment of specificity in every sample and eliminates potential interferences.

Follow-Up Testing

In order to test for defects in any of the enzymes involved in the pathway (see figure 1), tests for the precursor and the pathway product should be ordered.

Related Test

This panel replaces the RIA-based tests previously offered by ARUP (ARUP test codes 0070001, 0099606, and 0099725).

References

1. Antal Z, Zhou P. Congenital adrenal hyperplasia: diagnosis, evaluation, and management. *Pediatr Rev* 2009;30(7):e49–e57.
2. Merke DP, Bornstein SR. Congenital adrenal hyperplasia. *Lancet* 2005;365 (9477):2125–36.

Figure 1

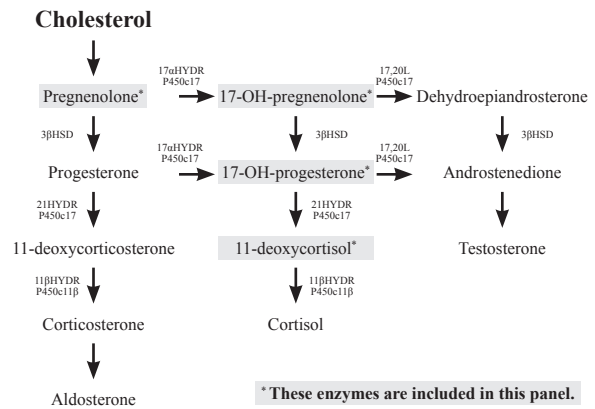
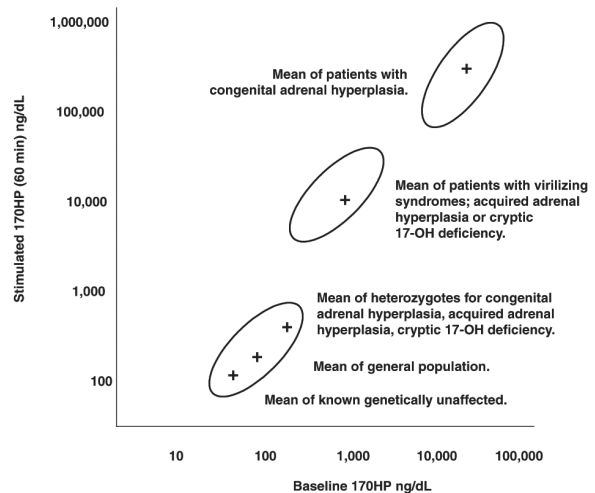


Figure 2



Test Information

0092330 Adrenal Steroid Quantitative Panel by LC-MS/MS, Serum or Plasma

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.
For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.

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