

# 17-Hydroxyprogesterone Analysis in Serum by LC-MS/MS

## HIGH SPECIFICITY LC-MS/MS TEST FOR 17-HYDROXYPROGESTERONE

### Test Highlights

17-Hydroxyprogesterone (17-OHP) serum levels are useful in the diagnosis of congenital adrenal hyperplasia (CAH) due to deficiency of 21-hydroxylase.

#### Disease Overview

- 17-hydroxyprogesterone (17-OHP, 4-pregnen - 17-ol-3,20-dione) is a steroid produced in the adrenals, gonads, and placenta. 17-OHP is a metabolic product of progesterone and 17-hydroxypregnenolone, and is a precursor to cortisol.
- A defect in 21-hydroxylase results in diminished cortisol biosynthesis, elevated ACTH, and accumulation of 17-OHP. 21-hydroxylase deficiency may lead to virilization due to increased adrenal androgen production and possible salt-wasting due to diminished production of aldosterone and deoxycorticosterone.
- 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 17-OHP.

#### Epidemiology

Approximately 90 percent of all cases of CAH are caused by 21-hydroxylase deficiency. In Caucasians, the severe form of CAH is detected in one in 10,000, and the mild form is observed in one in 1,000.

#### Genetics

When analyzing approximately 20 common mutations on chromosome 6p, it is possible to detect over 90 percent of all related defects. The remaining 10 percent of the mutations are rare and can only be detected with direct sequencing of the entire *CYP21* gene.

#### Pathophysiology

- 17-OHP is a precursor to cortisol. In patients with 21-hydroxylase deficiency, cortisol synthesis is diminished; however, because ACTH stimulates synthesis of the precursors to cortisol, the excessive production of other steroids involved in the pathway also occurs.

- 21-hydroxylase deficiency causes decreased concentrations of glucocorticoids and mineralocorticoids, as well as the excessive production of sex hormones.
- Clinical findings of the defect are masculinization, hypotension, and hyperkalemia.

#### Indications for Ordering

- The 17-hydroxyprogesterone (17-OHP) test should be used in patients with the following symptoms:

Salt-wasting crisis	Precocious Pubarche
Males and females with pseudohermaphroditism	Disordered puberty
Postnatal virilization	Menstrual irregularity
Hirsutism	Acne
Infertility	Hypertension

- This test should be used to monitor patients previously diagnosed with CAH due to 21-hydroxylase deficiency.
- In cases where the diagnosis is unknown, it is more appropriate to order a steroids panel (17-hydroxyprogesterone, 17-hydroxypregnenolone, pregnenolone, and 11-deoxycortisol), which would detect the deficiency of other enzymes causing CAH, such as 21-hydroxylase, 3β-hydroxysteroid dehydrogenase, 11β-hydroxylase, 17α-hydroxylase, and 17,20-lyase.

#### Additional Ordering Notes

- CAH may also be caused by the deficiency of other enzymes involved in adrenal steroids biosynthesis, such as 3β-OH-dehydrogenase, 17-hydroxylase, and 11β-hydroxylase.
- When CAH is suspected, a panel of steroids involved in the cortisol biosynthesis pathway should be tested in order to establish the specific enzyme deficiency.
- Please indicate the age and sex of the patient on the test request form and on the tube.
- The blood should be drawn early in the morning.

## Interpretation

- In most cases, a basal 17-OHP concentration within the normal reference interval rules out 21-hydroxylase deficiency.
- With some exceptions, basal 17-OHP above 300 ng/dL is suggestive of non-classic CAH, which can be confirmed with an ACTH stimulation test.
- Patients with basal 17-OHP above 300 ng/dL should have an ACTH stimulation test to confirm the presence of 21-hydroxylase-deficient non-classic CAH.
- False-negative results can occur due to a circadian decrease in ACTH and during the follicular phase of the menstrual cycle, as 17-OHP serum levels exhibit a diurnal pattern similar to cortisol and increase during the luteal phase of the menstrual cycle and during pregnancy.
- In figure 1, basal and post ACTH 17-hydroxyprogesterone concentrations are compared with those of normal subjects.
- The ratio of the basal 17-OHP to the post ACTH stimulation may be used to diagnose the enzyme deficiency (see figure 1 for results interpretation).

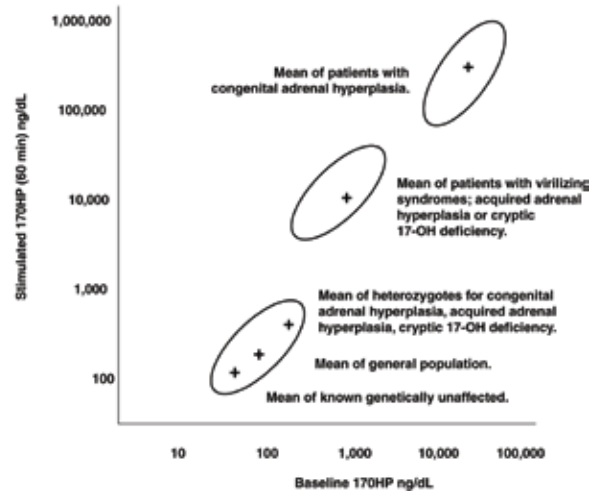
## Limitations

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

## Methodology

17-OHP is 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.

Figure 1



## References

1. Levine LS. Congenital adrenal hyperplasia. *Pediatr Rev* 2000;21:159–70.
2. Pang S. Congenital adrenal hyperplasia. *Endocr Metab North Am* 1997;26:853–91.
3. Pang S, et al. Pitfalls of prenatal diagnosis of 21-hydroxylase deficiency congenital adrenal hyperplasia. *Ann NY Acad Sci* 1986;458:111–29.
4. Pang S, et al. Prenatal treatment of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *N Engl J Med* 1990;322:111–5.

## Test Information

0092332

17-Hydroxyprogesterone Quantitative by LC-MS/MS, Serum or Plasma

For specific collection, transport, and testing information, refer to the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).