

The New Jersey Department of Health and Senior Services
Newborn Screening and Genetic Services

Congenital Adrenal Hyperplasia

Information for Health Professionals

Description

Congenital adrenal hyperplasia (CAH) is a common form of adrenal insufficiency inherited in an autosomal recessive manner. This group of diseases is due to mutations in the genes coding for several enzymes needed for the production of adrenal cortex hormones. A defect in the 21-hydroxylase enzyme accounts for 90-95 percent of CAH cases. This enzyme is necessary for efficient production of two vital adrenal steroid hormones: cortisol and aldosterone. The pituitary gland senses the cortisol deficiency and produces increased amounts of ACTH to stimulate cortisol production by the adrenals. The adrenal glands enlarge, but continue to produce inadequate amounts of cortisol. The precursor products of cortisol, some of which are virilizing hormones, accumulate and are released into the circulation. **Early detection and treatment is essential to prevent death in infants with salt-losing CAH.**

Incidence

The incidence is approximately 1:15,000-16,000. The incidence of congenital adrenal hyperplasia is especially high in Madagascar and certain areas of Alaska.

Clinical Features

Infants with CAH do not appear ill at birth, but may undergo a salt-losing crisis within the first weeks of life (usually between 6-30 days of age). A newborn with salt-losing CAH may have anorexia, vomiting, and dehydration accompanied by weight loss. Early symptoms can mimic other diseases such as sepsis, pyloric stenosis or reflux. Lethargy progresses toward coma; if not treated, affected newborns can die within days.

Early on, classic 21-hydroxylase deficiency results in the accumulation of 17alpha-hydroxy progesterone (17-OHP) and other hormones with androgenic properties, affecting the fetus. Female infants may appear normal at birth or may show the effects of virilizing hormones at birth. These include an enlarged clitoris and fusion of the labia majora over the vaginal opening. Male infants with CAH usually appear normal at birth, but may develop symptoms of dehydration within the first two weeks of life. Increased pigmentation of the nipples or scrotum may

be the only sign. If not treated, the continued excess of androgen precipitates rapid growth, inappropriately early puberty, and short adult height.

Screening

The screening test for CAH is part of the standard newborn screening. The test is a quantitative fluorometric assay for 17-hydroxyprogesterone (17-OHP), a precursor of cortisol. Factors affecting screening results include samples taken “too soon” (in the first 12 hours). These samples are more likely to show high 17-OHP levels than screening samples taken after the first day of life. Low weight (premature) babies also may have higher levels than term infants, which, in unaffected babies, should fall to normal over time.

Confirmatory testing

The confirmatory test is a serum 17-OHP, performed at a reference laboratory with accepted standards for infants. Repeat results of 17-OHP that are done by a “reference” laboratory have to be interpreted with caution, because many laboratories do not have normal references that are adjusted for age. This can create potential confusion in reporting units. Some laboratories are not accurate in determinations of endocrine tests in children. It is strongly suggested that all results be discussed with a pediatric endocrinologist. The level of 17-OHP on the screening test does not always correlate with the clinical severity of the disorder. Even a mild elevation in a term baby warrants a clinical evaluation and a serum 17-OHP as well as a serum sodium and potassium.

Treatment

The treatment of CAH is replacement hormone medications. The infant is given a glucocorticoid (a cortisol-like steroid medication). In addition, those who have aldosterone deficiency (salt-wasters), are given the mineralocorticoid fludrocortisone, which acts like the missing hormone aldosterone, enabling the body to retain salt. **Decisions about hormonal treatment should be made in consultation with a pediatric endocrinologist.** All patients need careful monitoring and lifelong medication adjustment to optimize growth, pubertal development and fertility.

Implications for genetic counseling

In families where one child is known to be affected with CAH, parents should be informed about how the disease is inherited and what their options are during subsequent pregnancies.

Interpretations/Recommendations Reporting ranges are weight dependent. *Interpretations/Recommendations only apply to filter paper screening test results. The normal ranges and units of measure used by commercial laboratories do not apply to filter paper results.*

Expected Results: No elevation of 17-OHP level

Borderline Results - Initial Specimen

<u>Birthweight</u>	<u>Result 17-OHP ng/mL</u>
<1250g	>135 - <160
≥1250g - <1750g	>90 - <135
≥1750g - <2250g	>65 - <90
≥2250g	>50 - <90

Recommend: Assess baby's health status: repeat filter paper sample within 2 days

Presumptive Positive Results - second borderline abnormal specimen

<u>Birthweight</u>	<u>Result 17-OHP ng/mL</u>
<1250g	>135 - <160
≥1250g - <1750g	>90 - <135
≥1750g - <2250g	>65 - <90
≥2250g	>50 - <90

Recommend: Immediate assessment of baby's health; consultation with a pediatric endocrinologist strongly recommended.

Presumptive Positive Results – Initial specimen

<u>Birthweight</u>	<u>Result 17-OHP ng/mL</u>
Initial Specimen:	
<1250g	≥160
≥1250g - <1750g	≥135
≥1750g - <2250g	≥90
≥2250g	≥90

Recommend: Immediate assessment of baby's health status; consultation with a pediatric endocrinologist strongly recommended

Interpretations/Recommendations (cont.)

Presumptive positive results - second presumptive positive specimen

<u>Birthweight</u>	<u>Result 17-OHP ng/mL</u>
<1250g	≥160
≥1250g - <1750g	≥135
≥1750g - <2250g	>65 - <90
≥2250g	>50 - <90

Recommend: Immediate assessment of baby's health status; consultation with a pediatric endocrinologist strongly recommended

Note: Newborn screening tests are an adjunct to clinical assessment, which is paramount. Congenital adrenal hyperplasia should be considered in infants with any of the signs.

Additional information:

Texas Department of State Health Services Newborn Screening
<http://www.tdh.state.tx.us/newborn/cah2.htm>

Illinois Department of Public Health Newborn Screening Program
<http://www.idph.state/HealthWellness/fs/congenitalhyper.htm>

American Academy of Family Physicians News & Publications
<http://www.aafp.org/afp/990301ap/990301b.html>

Johns Hopkins Medicine
<http://www.hopkinsmedicine.org/>

For questions, contact:

Inborn Errors of Metabolism Laboratory at (609) 292-3090
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