Congenital Adrenal Hyperplasia (CAH)
Information for Healthcare Professionals

Congenital adrenal hyperplasia refers to any of several autosomal recessive diseases resulting from mutations in genes coding for enzymes mediating the biochemical steps of production of cortisol from cholesterol by the adrenal glands. Most of these conditions involve excessive or deficient production of sex steroids and can alter development of primary or secondary sex characteristics in some affected infants, children, or adults. More than 90% of cases of congenital adrenal hyperplasia (CAH) are caused by 21-hydroxylase deficiency. The only form of CAH detected by Kansas Newborn Screening is 21-hydroxylase deficiency.

✓ Clinical Symptoms

The clinical phenotype depends on the nature and severity of the enzyme deficiency. There are three types of 21-hydroxylase deficiency. Two types are classic forms, known as the simple virilizing and salt-wasting types. In the third type of 21-hydroxylase deficiency, known as the nonclassic form, levels of functional 21-hydroxylase enzyme are moderate.

Female infants with 21-hydroxylase deficient CAH usually have some degree of virilization due to their exposure to excessive androgen levels in utero. Although male infants usually appear normal at birth, they may have an enlarged penis and scrotum with increased pigmentation. Symptoms of salt wasting CAH include frequent urination and, in some cases, poor feeding, which can rapidly progress to vomiting, dehydration, electrolyte changes and cardiac arrhythmia. **Infants with CAH who are not diagnosed and treated early are particularly susceptible to sudden death in the first few weeks of life.** In older children, CAH may result in rapid growth and precocious puberty with premature skeletal maturation.

✓ Incidence

The classic form of 21-hydroxylase deficiency appears in 1 in 15,000 – 25,000 newborns. The prevalence of the nonclassic form of 21-hydroxylase deficiency is estimated to be 1 in 100 individuals. The prevalence of both classic and nonclassic forms may vary among different ethnic populations.

✓ Genetics of congenital adrenal hyperplasia

Mutations in the CYP21A2 gene cause 21-hydroxylase deficiency. Mutations in the CYP21A2 gene are often caused by exchanges of DNA between the CYP21A2 gene and a pseudogene. These mutations alter the structure or production of the enzyme and cause 21-hydroxylase deficiency. Generally, mutations that only partially impair enzyme levels or function will have milder effects than more severe mutations that eliminate or greatly reduce the level of 21-hydroxylase enzyme.

✓ Inheritance Patterns

CAH is inherited in an autosomal recessive pattern. Parents of a child diagnosed with CAH are unaffected. These individuals are carriers of the condition and have one normal CYP21A2 gene and one abnormal CYP21A2 gene. Each pregnancy between carrier parents has a 25% chance of producing a child affected with CAH, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Treatment is life long and consists of glucocorticouid, and possibly mineralocorticoid, replacement. Additional doses are needed during times of stress, such as surgery or illness. The outcome is usually associated with good health, but short stature may result even with treatment. Males have normal fertility. Females may have a smaller opening of the vagina and impaired fertility.

✓ Screening Methodology

Newborn screening for CAH due to 21-hydroxylase deficiency is by fluorometric assay to measure the 17 hydroxy (OH) progesterone level. **Infants with a presumptive positive screening test (significantly elevated 17-OH progesterone level) require prompt follow-up.**

False positives are possible and may occur if the specimen is collected prior to 24 hours of age. Prematurity and illness can affect this screening, as physiological stress can cause a normal elevation of the 17-OH progesterone level. Treatment with hydrocortisone or dexamethasone may result in false negative screening results.

✓ **What to do After Receiving Presumptive Positive Congenital Adrenal Hyperplasia Screening Results:**
MEDICAL EMERGENCY: TAKE THE FOLLOWING IMMEDIATE ACTIONS:

1) **Contact family to inform them of the newborn screening result and ascertain clinical status.**
2) **Consult with pediatric endocrinologist or geneticist, having the following information available (sex, age at NBS sampling, birth weight) and refer, if needed.**
3) **Examine the newborn (ambiguous genitalia or non palpable testes, lethargy, vomiting, poor feeding).**
4) **Initiate timely confirmatory/diagnostic testing as recommended by specialist.**
5) **Emergency treatment as indicated (e.g. IV fluids, IM/IV hydrocortisone).**
6) **Educate family about signs, symptoms and need for urgent treatment of adrenal crisis.**
7) **Call KS Newborn Screening Program at 785-291-3363 with questions about results**
8) **Report Clinical Findings to Newborn Screening Program at 785-291-3363**
9) **Borderline abnormal (moderately elevated 17-OH progesterone) results require repeat filter paper screening as soon as possible.**

✓ **Confirmation of Diagnosis**

Diagnostic tests include serum 17-0HP (increased), serum electrolytes (reduced sodium and increased potassium), and blood glucose (reduced). Additional tests may be recommended by the specialist.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive Congenital Adrenal Hyperplasia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with congenital adrenal hyperplasia, the following points should be conveyed to parents:

- ***Parents should understand that treatment is lifelong and that compliance with medication and frequent blood monitoring are imperative to the child's health, growth and development.***
- ***Although children with CAH are usually healthy, any illness (for example, fever, vomiting or injury) requires prompt notification of the child's physician, as the cortisol dosage may need to be increased.***
- ***Parents should keep injectable hydrocortisone on hand at all times. If the child has repeated vomiting or is unable to hold down fluids, parents should call the specialist immediately. In emergencies, parents must be prepared to administer injectable hydrocortisone if instructed to do so by the physician.***
- ***Children and adolescents with CAH should wear medical identification bracelets or necklaces to alert health care providers to his/her condition and to insure proper medication is provided in an emergency.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, endocrinology, genetics and, in some cases, pediatric reconstructive surgery. Infants and children with congenital adrenal hyperplasia should have regular follow-up appointments with a pediatric endocrinologist to regulate medication regimens.***
- ***Parents who have a child with CAH have a 25% chance with each pregnancy of having another affected child.***

For consultation contact:

Kansas City Area
Pediatric Endocrinology
KU Medical Center
Office: 913-588-6326

Wichita Area
Wichita Endocrinology
Office: 316-777-6404

CMH – Wichita Specialty Clinic
Office: 316-500-8900

Topeka Area
Cotton – O'Neil Clinic
Office: 785-368-0460