

## What is congenital adrenal hyperplasia (CAH)?

The adrenal glands are located on top of the kidneys and produce several different hormones. *Congenital adrenal hyperplasia* (CAH) is a common inherited disorder in which the adrenal gland cannot make enough of a hormone, called *cortisol*, or a salt-preserving hormone, called *aldosterone*. The adrenal glands are located on top of the kidneys and produce several different hormones. Aldosterone helps the body hold onto sodium and release excessive amounts of potassium. In addition to cortisol and aldosterone, the outer portion of the adrenal gland (adrenal cortex) makes male-like hormones, called *androgens*. Some patients with CAH also cannot make enough aldosterone. The male-like hormones are responsible for the normal development of adult-type body odor, underarm hair, pubic hair, and adolescent acne. The inner portion of the adrenal gland (adrenal medulla) makes epinephrine, often called *adrenaline*.

The symptoms of the severe classic type of CAH are apparent at birth in girls in the form of a male-like genital appearance known as genital ambiguity; boys, however, often may not have any physical signs. Screening performed through newborn screening programs shortly after birth helps to identify most of these newborns. Other individuals do not develop symptoms until early childhood, the teenage years, or even adulthood. This form of CAH is called *non-classic* or *late onset*.

Cortisol is important for normal health and well-being. Symptoms associated with low cortisol levels are often nonspecific, but can include nausea, repeated vomiting, poor appetite, weight loss, and fatigue. Symptoms associated with low aldosterone levels may include low blood pressure, dehydration, low blood sodium (salt) levels, and high blood potassium levels.

The adrenal gland cannot make enough cortisol or aldosterone in classic CAH; instead, it makes large amounts of extra male-like androgen hormones. High levels of androgen hormones can alter the appearance of the external genitals of newborn girls to look more like those of a newborn boy (a condition known as *virilization*). In such cases, newborn girls may have an enlarged clitoris, labia (the lips around the opening of the vagina) that are fused together, or genitals that look very similar to those of a boy, except that the testicles are missing. Baby boys with CAH usually have normal male external genitals; their testicles are located in their scrotum.

Young children with non-classic CAH may develop pubic hair at ages younger than normal or may develop enlargement of the clitoris or penis. Teenaged and adult women with non-classic CAH may present for medical care because of irregular menstrual periods or excessive body hair (hirsutism).

## How common is CAH?

The most common type of CAH is caused by 21-hydroxylase deficiency due to abnormalities in the 21-hydroxylase (*CYP21A2*) gene. This gene tells our bodies how to make the 21-hydroxylase protein. When the 21-hydroxylase protein is absent or does not work normally, the adrenal gland cannot make enough cortisol. For some patients, the adrenal gland cannot make enough cortisol or aldosterone.

Congenital adrenal hyperplasia is an autosomal-recessive condition. This means that affected individuals have inherited one abnormal *CYP21A2* gene from each parent. The parents are usually not affected but are known as carriers of the disease trait or *heterozygotes*. To have the physical signs and clinical symptoms of CAH, newborns need to inherit one affected gene from each parent. For autosomal-recessive disorders, there is a 25% chance of having an affected child in each pregnancy if each parent is a carrier of the disease trait.

In the general population, the most severe form of CAH (classic 21-hydroxylase deficiency) occurs in approximately 1 in 15,000 people. The milder non-classic form of CAH is more common and occurs in approximately 1 in 1,000 people. The different types of CAH are caused by differences in the specific *CYP21A2* gene defects.

## How is CAH diagnosed?

The diagnosis of CAH is often suspected in newborns with male-like (ambiguous) external genital development. All states in the United States perform newborn screening blood tests for classic 21-hydroxylase CAH caused by a deficiency of the 21-hydroxylase enzyme because of the possibility of severe salt loss, dehydration, or misidentification of gender (a girl being thought to be a boy) in these newborns shortly after birth. The newborn screening test measures the level of 17-hydroxyprogesterone (17-OHP) in a blood sample. 17-OHP is a hormone that is normally made into cortisol in unaffected people but is overproduced in patients with CAH.

When doctors are concerned that a newborn might have CAH, several additional tests are done. One test is a repeat blood 17-OHP level. Other hormone levels are also often measured, and the baby's blood sodium and potassium levels are measured. Sometimes, ultrasound imaging is performed. In some patients, especially older children, adolescents, and adults, a special blood test known as an adrenocorticotropic hormone (ACTH)O or Cortrosyn stimulation test may be performed to look for milder forms of CAH. This test involves collection of an initial blood sample, administration of synthetic ACTH hormone through an intravenous line, and collection of a second blood sample. An elevated 17-OHP level confirms the diagnosis of CAH. Genetic testing may be helpful, but hormone measurements are the most helpful diagnostic tests.

## How is CAH treated?

veloping normally and is given the most appropriate hormone replacement treatment. With appropriate hormone therapy, typical growth, development, and fertility are highly possible.

Individuals with classic CAH must take extra cortisol dosages when they are sick to maintain health. Your child's physician will teach you when and how to increase the cortisol dose. Your child's physician will also teach you how to administer cortisol by an intramuscular injection (eg, Solu-Cortef, Hydrocortisone sodium succinate) when your child is unable to take the medication by mouth. Individuals with CAH should wear medical alert identification badges. Although many patients with non-classic CAH may not need to take daily cortisol replacement dosages, they may need to take cortisol replacement dosages during a major illness, such as high fevers or during periods of significant physical stress.

### Can CAH be prevented?

CAH cannot be prevented. In the past, an experimental medication was prescribed for pregnant women who were at risk for having a newborn girl with CAH to prevent the overgrowth of the clitoris and atypical external geni-

tal appearance. This experimental medication does not cure CAH. In addition, current information indicates that this treatment may have negative effects in later life and is no longer recommended.

Families concerned about their risk of having another child with CAH should discuss this concern with their child's endocrinologist in consultation with a genetic counselor.

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