Congenital Adrenal Hyperplasia

Hormone Health NETWORK®

A PATIENT'S GUIDE

Congenital adrenal hyperplasia (CAH) is a genetic disorder of the adrenal glands that affects about one in 10,000 to 15,000 newborns, both male and female. The adrenals, which sit on top of the kidneys, make steroid hormones that are necessary for healthy body functions. Normally, the adrenals produce *cortisol* (a glucocorticoid), *aldosterone* (a mineralocorticoid), and *androgens* (male sex hormones).

- **Cortisol** is essential to life in that it helps the body use food for energy and helps maintain blood sugar levels. It is called a "stress" hormone because the adrenals make more of it when we are under physical or emotional stress, protecting us from the effects of illness and injury.
- **Aldosterone** helps keep normal levels of salt and water in the body. With low aldosterone, salt and water are lost in the urine, leading to dehydration. Aldosterone also regulates blood volume (the amount of blood circulating in the body) and blood pressure.
- **Androgens** help regulate body growth and the development of underarm and pubic hair in males and females and masculine features in males.

The most common form of CAH results from having too little cortisol and aldosterone and having too much androgen.

CAH is caused by a defect in the genes that control the production of certain enzymes. Enzymes are proteins that increase the rate of chemical reactions in the body and are needed to produce adrenal hormones. The enzyme most commonly lacking in CAH is 21-hydroxylase (21-OH). For this reason, CAH is sometimes called *21-OH deficiency* and can be severe, moderate, or mild. This patient guide is based on clinical guidelines developed by The Endocrine Society to provide doctors with the most up-to-date scientific information on managing CAH.

Who is affected by CAH?

Children inherit genes from their parents, getting one copy of each gene from each parent. A child is more likely to be born with CAH if both parents have the disorder or are *carriers* of the gene defect. A carrier has a pair of genes in which one is normal and the other is defective. Carriers can pass the defective gene on to their children, but do not have CAH themselves. Some ethnic groups are more likely to develop this disorder, such as European Caucasians for the severe form of CAH and Ashkenazi (Eastern European) Jews for the mild form.

What are the effects of 21-OH deficiency?

CAH is classified as *classic* or *nonclassic*, according to the degree and effects of the 21-OH deficiency.

Classic CAH has two forms—salt-wasting and simple virilizing (also called non-salt-wasting).

- **Salting-wasting CAH** (so called because the body has trouble keeping the right amount of salt in the blood) is *severe* 21-OH deficiency. With this form of CAH, levels of both cortisol and aldosterone are reduced, and androgen is increased.

  Salting-wasting CAH is the most common cause of ambiguous genitalia in newborn females. That is, the baby girl's external sex organs look both male and female. However, her internal female reproductive organs (ovaries, uterus, fallopian tubes) are normal. Male newborns with salt-wasting CAH do not have ambiguous genitalia, although they might have an enlarged penis.

  Excess androgens also cause virilization (development of masculine features) in girls or boys before the age of puberty. Some examples of virilization are development of pubic hair, rapid growth, and increased muscle strength.

  Salt-wasting CAH can cause life-threatening vomiting, weight loss, and dehydration in the first weeks of life. To prevent this type of crisis, babies are tested for CAH shortly after birth in most developed countries.
- **Simple virilizing (non-salt-wasting) CAH** is *moderate* 21-OH deficiency. With this form of CAH, levels of cortisol are reduced, but the degree of aldosterone deficiency is not as extreme, and there is no salt-wasting. This form of CAH causes ambiguous genitalia in baby girls and virilization in both sexes before puberty.

Nonclassic CAH has one form and is considered a *mild* 21-OH deficiency. With this form of CAH, neither cortisol nor aldosterone is greatly reduced, and again, no salt-wasting occurs. There are androgen effects, but newborn girls usually have no genital ambiguity. The signs and symptoms of nonclassic CAH may not appear until early childhood or later. The excess androgen can affect growth, puberty, and fertility, but to a lesser degree than with classic CAH.

How is CAH diagnosed?

Classic CAH is often diagnosed at birth or soon after. All newborns should be tested for 21-OH deficiency. Diagnosis of CAH is based on a blood test that measures a hormone related to cortisol production (17-OHP). If that screening test is positive, then further tests should be performed as soon as possible to determine whether the newborn has CAH.

Nonclassic CAH is often not detected in the newborn test and therefore, may not be diagnosed until childhood or adulthood. Diagnosis in childhood or later may be based on a physical exam and family history, as well as blood, urine, and possibly genetic tests.

Is prenatal diagnosis and treatment a possibility?

CAH can be diagnosed in a fetus, and in some cases the drug dexamethasone has been given to pregnant women to lessen the virilization of affected females. Giving dexamethasone to a pregnant woman whose baby may have CAH is controversial because there is limited scientific knowledge about the long-term effects of this treatment on the baby. The Endocrine Society guidelines consider prenatal treatment experimental and do not recommend it, except in approved clinical trials (research studies that involve people).

How is CAH treated?

Treatment of classic CAH starts soon after birth and is needed life-long. People with classic CAH should have a team of health care providers, including specialists in pediatric endocrinology, pediatric urologic surgery (for girls), psychology, and genetics. Still, other than having to take daily medication, people with classic CAH can have a normal life. People with nonclassic CAH may not need any treatment, or may not need life-long treatment, depending on their symptoms. Treatment must be individualized under the care of doctors experienced in treating this condition.

Classic CAH

Medical treatment: The goals are to reduce excess androgen production and replace the missing hormones. Proper treatment with glucocorticoids prevents "adrenal crisis" (a life-threatening condition that occurs when there is not enough cortisol and aldosterone) and virilization. Treatment allows normal growth and development.

Treatment with glucocorticoids is a balancing act. Undertreatment carries the risk of adrenal crisis and allows increased androgen production. Excess sex hormones can cause bones to mature too soon and stop growing, which can mean that adult height is less than average. Undertreatment can also disrupt normal puberty and reproductive function. Overtreatment can suppress growth, increase blood pressure, and cause other health problems linked to excess cortisol, such as obesity, low bone density, and high blood glucose (sugar).

For growing patients with classic CAH, treatment includes glucocorticoids (most often hydrocortisone tablets) to replace cortisol and mineralocorticoids (fludrocortisone tablets) to replace aldosterone. Sodium chloride (salt) supplements are also recommended for newborns and infants. Older patients who are no longer growing still need to take glucocorticoids, but they can take hydrocortisone, prednisone, or dexamethasone. The latter two drugs are longer-acting and more potent.

In times of illness accompanied by high fever, surgery, or major injury, CAH patients of all ages need close medical attention. At these times, more cortisol is needed to help recovery and to keep up with the body's increased demands. For pregnant women with CAH, higher doses of glucocorticoids are usually used during labor and delivery.

Surgical treatment: Surgery to correct ambiguous genitalia is thought to be easier when performed soon (within months) after birth. This procedure should only be performed by an experienced surgeon in a center with similarly experienced pediatric endocrinologists and support staff.

Nonclassic CAH

Unlike classic CAH, nonclassic CAH is mild and not life-threatening. People with nonclassic CAH who have no symptoms do not require treatment or genital surgery.

Treatment with glucocorticoids is recommended in children with very early puberty and maturing of bones (which may put them at risk for mild short stature) and in girls who develop masculine features such as hirsutism (male pattern hair growth on the face and body) or deep voice or who have irregular or absent menstrual periods. Treatment may be stopped when the symptoms go away. For women with hirsutism, medical treatment may include an oral contraceptive. People with nonclassic CAH and fertility problems can sometimes conceive when treated with glucocorticoids.

How is CAH treated during pregnancy?

Pregnant women with CAH should be under the care of endocrinologists and obstetricians. Women with CAH who become pregnant should continue their pre-pregnancy doses of glucocorticoids (hydrocortisone and prednisone, but not dexamethasone, which can affect the fetus) and mineralocorticoids. Physicians will adjust doses if needed.

What can you do to help the treatment process?

You and your doctor or your child's doctor should be partners in the treatment process. You should keep regular appointments with an endocrinologist so your or your child's condition can be monitored, and you should let the doctor know of any changes in health. It is essential that medications be taken regularly.

People who require treatment should always wear or carry medical identification stating that they have adrenal insufficiency (lack of adrenal hormones) and in an emergency should be given additional hydrocortisone, usually by injection.

People with CAH may have problems with maintaining a healthy weight, high blood pressure, and insulin resistance (when the body has trouble using insulin properly). It is important to follow a healthy lifestyle with a balanced diet and daily exercise to avoid the serious health risks associated with these conditions.

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Note to health care professionals: This patient guide is based on, and is intended to be used in conjunction with, the Endocrine Society's clinical practice guidelines (available at www.endocrine.org/guidelines/index.cfm).