What is CAH?

Congenital adrenal hyperplasia (CAH) is a disease caused by lack of an enzyme that is important for production of one or more of the steroid hormones made in the adrenal glands. The adrenal glands are glands that sit on top of your kidneys. The adrenal glands make 3 types of steroid hormones: mineralocorticoids, cortisol (hydrocortisone), and androgens. Mineralocorticoids (the main hormone is aldosterone) control salt balance in your body. Hydrocortisone is a natural steroid termed a “glucocorticoid.” The amount of hydrocortisone in the blood normally rises in the early morning and whenever you are sick or stressed. It maintains your body’s homeostasis (equilibrium) and is essential for life. People with low hydrocortisone (cortisol) levels can have low blood pressure, nausea, vomiting, and muscle aches and pains. Androgens are sex hormones and are responsible for hair under the arms and in the pubic area as well as for enlargement of the penis and increase in size of the female equivalent, the clitoris. In most kinds of CAH, the adrenal gland is not able to make cortisol but instead makes too much androgen. CAH is a congenital and inherited disorder. Inheriting 2 abnormal genes—one from each parent—for an enzyme (a protein) that is needed to make cortisol leads to CAH. The most commonly affected enzyme is produced by the 21-hydroxylase or CYP-21 gene. Absence of this enzyme results in very high levels of 17-hydroxyprogesterone.

In the most severe form of CAH caused by 21-hydroxylase deficiency (salt-wasting), patients will lose too much salt in their urine because they do not make enough mineralocorticoids. Girls may be virilized from too much male hormone (androgen), and their external genitals may have some male characteristics. In the non–salt-wasting form, which is milder, children are able to maintain salt balance but still have too much androgen. Both types usually cause symptoms within days to weeks after birth. A much milder form presents later in childhood with early pubic hair or adult type body odor. This is called nonclassical CAH.

How is CAH diagnosed?

The classical form of CAH (salt-wasting and non–salt-wasting) is tested for in the newborn blood screening in every state in the United States. The newborn screening measures the level of 17-hydroxyprogesterone, a hormone that is eventually made into cortisol in unaffected people. In the most common form of CAH, 17-hydroxyprogesterone cannot be broken down effectively and it builds up to very high levels, which can be measured to make the diagnosis. In baby boys, the disease is not usually suspected at birth. The diagnosis is made when the newborn screening results come back high or the baby becomes sick in the first week to month of life. In a baby girl, the diagnosis may be suspected if her external genitals show evidence of exposure to high levels of androgen. In such a case, the infant may have an enlarged clitoris, labia that are fused together, or genitals that look very similar to a male except that the testicles are missing. If an infant has genitals that have an appearance in between that of a normal boy and a girl (large clitoris and vaginal opening that is closed off) or the newborn screening result for CAH comes back high, your baby’s doctor will draw blood from your infant to measure the level of 17-hydroxyprogesterone and the salt level. Sometimes, other hormones are measured as well.

How is CAH treated?

Because the basic defect is a block in the synthesis of the glucocorticoid hormone hydrocortisone (sometimes called cortisol), the main treatment for classical CAH is to give a glucocorticoid hormone as replacement. The most common medication used is called hydrocortisone. This is usually given 3 times per day. Another hormone with mineralocorticoid action called fludrocortisone is also used to help the body retain sodium (salt) and get rid of potassium in the urine. Sometimes in infants, extra salt is also given. Because people with classical CAH cannot make cortisol (hydrocortisone) efficiently, they must take extra hydrocortisone when they are sick to maintain health. This is very important to remember, because someone with classical CAH who is nauseated, is vomiting, or requires surgery and does not get extra glucocorticoid may become very sick. Patients with nonclassical CAH can make cortisol normally, so they do not always need treatment. If patients with nonclassical CAH have significant effects from too much androgen, they are sometimes treated with a small dose of glucocorticoids like hydrocortisone or prednisone.

How common is CAH?

In the general population, the most severe form of CAH (classical) occurs in approximately 1 of 15,000 people. This is an autosomal-recessive condition and requires that a defective gene be inherited from each parent, but the parents, who are called carriers, are not affected. When both parents have a defective gene, there is a 25% chance of having an affected child in each pregnancy. The nonclassical form of CAH may be much more common, particularly in some populations.
Can CAH be prevented?

CAH cannot be prevented. However, experimental treatment is available for pregnant women who are carrying affected female fetuses. This involves treating the pregnant mother with a synthetic glucocorticoid as soon as she knows that she is pregnant. This treatment may result in decreased male hormone levels in the fetus and, therefore, less abnormal genitals. Because all of the side effects are not fully known, and the same treatment might affect brain cell development, this remains an experimental and controversial treatment.

Kathleen Bethin, MD, PhD, FAAP, and
Teresa Quattrin, MD, FAAP
PES/AAP-SOEn Patient Education Committee