Congenital Adrenal

Congenital Adrenal Hyperplasia (CAH) is a genetic disorder of the adrenal glands. People with CAH cannot make enough of certain essential hormones, particularly cortisol and aldosterone. At the same time, the body produces an excess of androgens such as testosterone, which can cause male characteristics to appear early or inappropriately. The most common cause of CAH is loss of an enzyme called 21-hydroxylase, or CYP21. Symptoms depend on the type and degree of mutation and are worst when cortisol and aldosterone levels are lowest.

Classic congenital adrenal hyperplasia is the more severe form of the disease and is usually detected in infancy or early childhood. The most obvious sign in girls is abnormal genitals that look more male than female, which may include an enlarged clitoris—a condition called ambiguous external genitalia. Boys tend to appear normal at birth, though some affected male infants have an enlarged penis. Additional symptoms develop within two to three weeks after birth, including poor feeding, vomiting, dehydration, and an abnormal heart rhythm. Patients of any age with classic CAH are in danger of experiencing a life-threatening "adrenal crisis," which can result in a low blood sugar and salts, diarrhea, vomiting, dehydration, and shock. People in an adrenal crisis need immediate treatment.

Nonclassic congenital adrenal hyperplasia is a milder form and usually develops in late childhood or early adulthood. Girls with nonclassic CAH may experience abnormal menstrual periods (or lack of menstruation), early appearance of body hair, excessive growth of facial hair, and some enlargement of the clitoris. Despite having normal ovaries, uterus, and fallopian tubes, these women may be infertile. Boys with the milder form appear normal at birth but appear to enter puberty early, including a deepening voice, early appearance of body hair, enlarged penis but normal testes, and well-developed muscles.

All children with CAH tend to experience very early puberty and grow tall quickly, but they will have a much shorter-than-average final adult height. Women often have irregular menstrual cycles. In both females and males, long-term complications of CAH can include infertility, high blood pressure, low blood sugar, severe acne, low bone density, high blood cholesterol, and obesity. Sexual problems are likely, such as pain during intercourse, embarrassment about genitals, and discomfort telling a new partner about the disease.

Inheritance

CAH is passed along in an inheritance pattern called autosomal recessive, which means that both copies of a child's gene need to be defective in order to develop the disease. The parents of child with CAH have inherited only one copy of the gene which has a change in it that stops it from working properly (faulty gene). They are called carriers of disease. Being a carrier does not cause health problems, because the second, working, copy of the gene acts as a "back-up." This type of genetic change is called recessive, because the second, working, copy of the gene can compensate for the non-working copy. If two people who are carriers for CAH gene have children, there is a 25% (1 in 4) chance that they could both pass on the copy of the CAH gene which is not working. When a child inherits two non-working copies of the CAHgene, one from each parent, then there is no "back-up," so he or she would have CAH. When a child is diagnosed with CAH, the parents are presumed to be carriers of this condition. Depending on the mutation, the child's symptoms can vary from clinically silent to mild non-classic CAH to severe classic CAH. Parents with a family history of CAH or a child who has the condition should consider genetic counseling.

Hyperplasia (CAH)

Diagnosis

Classic CAH is usually detected clinically at birth or in early infancy. In nonclassic congenital adrenal hyperplasia, parents may notice signs of early puberty in a toddler or young child. Occasionally, symptoms do not develop until teenage or young adult years.

Once CAH is suspected, blood and urine tests can be used to measure abnormally low levels of salts, cortisol, and aldosterone produced by the adrenal glands, as well as unusually high levels of androgen hormones. A pelvic ultrasound may be performed on an infant with ambiguous genitalia to determine if the baby has a uterus, cervix, and fallopian tubes. Alternately, an analysis of the baby's chromosomes—called karyotyping—can determine the genetic sex of the child. In toddlers and children, X-rays may show advanced skeletal maturation, indicating that the child's bones appear to be older than their actual age.

Prenatal diagnosis is available for some forms of CAH by amniocentesis or chorionic villus sampling. These tools are used most often when siblings have the disease or family members are known to carry the mutation. Treatment can then be started in the womb, which may reduce the risk of later complications. Even if there is no known history of CAH, a neonatal screening test for 21-hydroxylase deficiency can be done on heel-stick blood as part of the standard newborn screening programs. This test is routinely performed in many countries, as it may be lifesaving for an affected male infant who would otherwise be undetected until presenting with a dangerous adrenal crisis.

Management

Although CAH can be life-threatening, proper treatment allows most people to manage it well and lead normal lives. Affected persons suffering from an adrenal crisis need prompt intervention with sugars and rehydration fluids. On a long-term basis, patients should take replacement steroid hormone medication daily. Close management by a doctor is critical: additional doses may be needed during times of stress, such as severe illness or surgery, and overdoses may cause serious side effects.

In some infant girls who have ambiguous external genitalia, doctors recommend reconstructive surgery at two to six months of age to correct the appearance and function of the genitals. This procedure may involve reduction of the clitoris and reconstruction of the vaginal opening. If CAH is diagnosed in a fetus, prompt treatment can reduce or even eliminate symptoms after birth. The pregnant mother can take a powerful corticosteroid that crosses the placenta to suppress the over-excretion of testosterone, allowing female genitals to develop normally and reducing masculine features that may develop later in female fetuses.

CAH in Arab Populations

CAH is a spectrum disease, which means that cases range from clinically silent to severe, with multiple different symptomatic presentations. This makes it difficult to accurately estimate the number of babies born with this condition. Depending on the population, the more severe classic CAH is found in 6 to 10 babies per 100,000 live births in Western countries. Rates in Middle Eastern countries are mixed: Qatar records only 4 affected infants per 100,000 births, while studies reveal 10 to 18 per 100,000 in Oman and 11 to 14 per 100,000 in Kuwait. Although population-wide data is not available in all countries, CAH has been documented in Egypt, Jordan, Saudi Arabia, Tunisia, and the UAE. Cases of a rare but serious form of this disease called lipoid CAH have been reported in Libya, the Palestinian territories, Qatar, Saudi Arabia, and Yemen.