Congenital adrenal hyperplasia (CAH)

Summary

- CAH is a fairly uncommon genetic disorder, but one which is well understood and for which good treatment is readily available.
- CAH is a congenital disorder (present at birth) involving the hormones of the adrenal glands.
- The adrenal glands produce cortisol, salt-retaining hormone and androgen.

Congenital adrenal hyperplasia (CAH) is a rare genetic disorder, but it is well understood and treatment is readily available. CAH is also a congenital disorder (present at birth) involving the hormones of the adrenal glands. The word ‘hyperplasia’ means ‘overgrown’. A child with CAH is born with overgrown adrenal glands.

Adrenal glands explained

The adrenal glands are a pair of fleshy triangular-shaped organs, each about the size of a walnut, which lie above the kidneys, on the back wall of the abdomen. Although fairly small, the adrenal glands make some of the most important hormones that the body cannot do without, including cortisol. These hormones are available in tablet or injection form, so that the adrenal glands themselves can be done without if necessary.

In children with CAH, there is a problem with the complex chemical ‘machinery’ needed to make those essential hormones.

Control of the adrenal glands

The adrenal glands are controlled by the pituitary gland, a pea-sized gland at the base of the brain. It is the ‘master gland’ that directs many of the other glands. When the adrenal glands are not producing enough of their main hormone (cortisol), the pituitary tells them to make more by sending an adrenal-stimulating hormone.

If the levels of adrenal-stimulating hormone remain high for too long, the adrenal glands grow larger. When too much cortisol reaches the pituitary, the pituitary switches off the adrenal glands, so they are allowed to rest until the hormone levels return to normal. Usually, the pituitary and the adrenal glands are perfectly balanced.

Types of hormones

Hormones are the chemical messengers in the body. They are produced in one place by an endocrine (or hormone-producing) gland, and act somewhere else in the body. Female sex hormone (oestrogen), for example, is made in the ovaries and acts elsewhere to cause breast enlargement, broadening of the hips and menstrual periods.

There are many different types of hormones and many endocrine glands, each making its own special hormones. In trying to understand CAH, the most important glands to consider are the adrenal glands and the pituitary gland.

Adrenal hormones

The adrenal glands produce cortisol, salt-retaining hormone and androgen. Not only are the adrenal glands each able to make all three hormones, but they make them from the same starting material – cholesterol. This can be made in the body, but is also found in the diet, in animal fats.

CAH results in three disturbances to these hormones:

- lack of cortisol
- lack of salt-retaining hormone
- too much androgen.
Cortisol
Cortisol is needed to protect the body from the effects of illness or injury. If a person with poorly functioning adrenal glands develops an illness such as tonsillitis, or receives a significant injury such as a broken leg, they could go into a state of ‘shock’ (severe illness with dangerously low blood pressure) unless cortisol or an equivalent medication (such as cortisone) is given.

Salt-retaining hormone
This governs the amount of salt lost in urine via the kidneys. In the absence of this hormone, salt is lost uncontrollably, leading to dehydration and lack of salt.

Androgen (male sex hormone)
Both males and females have androgen. It is thought to aid growth in childhood and is responsible for women having pubic hair.

CAH non-salt losers and salt losers
Children with CAH are classified as either non-salt losers (20 per cent of CAH patients), or salt losers (80 per cent).

Non-salt losers
Children with non-salt-losing CAH are usually healthy, but may be born with genital abnormalities resulting from an excess of androgen. In girls, non-salt losing CAH is usually diagnosed at birth because the clitoris is large and the labia are partially fused. Sometimes, however, the changes may not be very obvious. In cases where the diagnosis is not made at birth, the growth of the clitoris continues and becomes much more obvious as time goes by.

In boys, non-salt-losing CAH produces nothing that can be detected at birth. Usually, the diagnosis is made when very prematurely the boy’s penis enlarges, perhaps he grows some pubic hair, and he becomes unusually tall. These changes may not be noticed until two to three years of age. They all result from premature exposure to excessive levels of androgen. X-rays show advanced maturity of the bones.

This is undesirable, and indicates that the child is closer to completion of growth than he should be. Some growth that should occur during childhood is lost. Because of this, adult height is usually somewhat reduced in people with this condition.

Salt-losers
In salt-losers, the deficiency in the adrenal glands is more severe than in non-salt losers. Their strong tendency to lose excessive amounts of salt in the urine, if uncontrolled, can cause acute dehydration, very low blood pressure, nausea and vomiting. The levels of salt (sodium and chloride) and sugar (glucose) in the blood fall, and the potassium level rises. This dangerous situation is referred to as an ‘adrenal crisis’. Very urgent medical treatment is needed as a life-saving measure.

Some people with the salt-losing form of CAH receive very little warning of adrenal crises. Repetitive vomiting is often the first sign. Drowsiness is most likely to be due to an abnormally low blood sugar level, and if sugar is not given, may progress to loss of consciousness.

Non-salt-losers hardly ever experience adrenal crises because they make more cortisol and more of the salt-retaining hormone than the salt-losers.

Causes of an adrenal crisis
The body usually responds to sickness (fever, infection or other illness) and physical injury by releasing more cortisol. This helps to boost the blood sugar and blood pressure, aiding recovery. In CAH, the adrenal glands are unable to make more cortisol.

Therefore, the body is less protected and the effects of illness or injury may be more severe. Adrenal crises can be readily prevented.

Treatment of CAH
CAH is a lifelong disorder for which no cure is available. It is possible, however, to readily replace, in tablet form,
the hormones that are missing – cortisol and the salt-retaining hormone. These medications will be needed every day for life, and need to be given even when the child is perfectly well. There is no need for a special diet with CAH. Girls with CAH require surgery to restore the genital appearance to normal. Boys do not.

There are several medications available that are satisfactory substitutes for the natural hormone, cortisol. They are hydrocortisone, cortisone, prednisolone and dexamethasone. They differ in potency (strength) and duration of action. If a salt-retaining hormone is needed, fludrocortisones are used.

Dexamethasone is generally considered unsuitable for use in growing children because its high potency and very long action (24–48 hours) interferes with growth. Once adult height has been reached, however, dexamethasone provides excellent 24-hour control, with the added advantage that it needs to be taken only once a day.

Blood tests may be required every three months throughout childhood to help monitor replacement medication therapy. An injection of cortisone (hydrocortisone) may be required if a person with CAH becomes very sick or needs surgery.

**When to give extra cortisone**

Extra cortisone is not necessary with minor cuts and scratches, even if local anaesthetic (an injection near the cut to deaden sensation) is proposed. However, if the injury is more severe (such as a broken arm or leg), extra cortisone should be given.

Other times to use extra cortisone include:

- when your child feels ill, particularly if he or she has a high temperature
- when your child requires a general anaesthetic for any reason. It is absolutely essential that he or she is given an injection of cortisone beforehand. Failure to do this could cause death
- when your child is vomiting, or has diarrhoea. Not only does the child have to cope with the extra demands of being ill, but also the stomach may not absorb the medications needed to treat the CAH in the usual way. Your child may need to be given an injection of cortisone. Severe vomiting or diarrhoea in someone with CAH is often best treated in hospital.

Consult your doctor about how much extra cortisone to give your child. If you are in doubt when to give extra cortisone, it is always safer to give it, than not to give it.

**Advice for people with CAH**

Precautions for people with CAH include:

- Every person with CAH should wear an identification disc or bracelet carrying the words, ‘Adrenal insufficiency: In emergency, give cortisone’.
- If you plan to travel, it is a good idea to ask your child’s specialist for a letter outlining the important medical problems that your child could have, and how these should be dealt with in an emergency.

**Genital changes in girls with CAH**

In baby girls with CAH, the genitalia may look more masculine than they should. The clitoris is enlarged and may resemble a small penis. In addition, the cleft between the labia or lips may be partly closed over, hiding the entrance to the vagina. Often, only one opening can be seen. The urinary passage and vagina both open into this one entrance.

The internal organs, however, are quite normal. The vagina, uterus (womb) and ovaries are perfect, and girls with CAH are usually able to have children.

Sometimes, it is difficult to be sure about a CAH baby’s true sex at the time of birth. Tests to determine what internal organs are present may be needed, as well as hormone tests related to the adrenal glands. The results of these tests can usually be obtained within two to three days.

**Surgical treatment for girls with CAH**

Girls with CAH may need surgery to reduce the size of the clitoris to normal, separate the fused labia and enlarge
the vaginal entrance. The technical name for this operation is ‘clitoral recession or reduction and vaginoplasty’. It is
done either in one or two stages.

The clitoral reduction or recession is done is the first few months of life. The vaginoplasty is sometimes done at the
same time as the clitoral reduction, but may be left until adolescence, before the menstrual periods begin. Some
stretching of the vagina may be necessary later to allow menstruation and comfortable sexual intercourse. The
female hormones made by the ovaries at puberty soften the tissues and make the stretching easier.

Adult life for women with CAH
Women with CAH can have children of their own and there is little difficulty becoming pregnant, provided that the
hormone balance is kept under good control. If the hormones are not well balanced (perhaps due to forgetting to
take medications), the menstrual periods may become irregular or even temporarily cease.

Because nearly all girls with CAH have had surgery around the vagina as children, there is scar tissue there. This
may not stretch enough to allow vaginal delivery, and it is therefore sometimes necessary for a Caesarean
operation to be performed to deliver the baby. Extra cortisone will be needed during labour and delivery.

How CAH is inherited
CAH is a genetic disorder resulting from one of the more common recessive gene defects. In fact, about one
person in 50 in the general population has a CAH recessive gene hidden away among the many thousands of
genes they possess, and yet only one person in 10,000 has CAH.

People with CAH have received a CAH gene from each of their parents. Because their cells only contain two
abnormal recessive CAH genes and no normal ones, the cells in the adrenal glands are unable to make the
enzyme in normal amounts, and this has a major effect on the way the adrenal glands work.

If a couple already has one or more children with CAH, and neither parent has CAH, the chance with each
subsequent pregnancy that the child will have CAH is one in four. If a person with CAH marries a person without
CAH, the chance of their having a child with CAH is very low, about one in 100. If two people with CAH marry, all of
their children would have CAH.

Where to get help
- Your doctor
- Endocrinologist
- Congenital Adrenal Hyperplasia Support Group of Australia Inc. Tel. (03) 9513 9255

Things to remember
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  readily available.
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