ENDOCRINE DISORDERS:
CONGENITAL ADRENAL HYPERPLASIA (CAH)

What is Congenital Adrenal Hyperplasia?

CAH is an inherited condition that affects the adrenal glands and causes a number of specific health issues.

'Congenital' means the condition is present at birth. The adrenal glands are cone-shaped organs that sit on top of each kidney. They make a number of hormones necessary for healthy body function. Hyperplasia means 'overly large'. In people with CAH, the adrenal glands cannot make enough of a hormone called cortisol. As they start working harder in attempts to make more cortisol they increase in size, resulting in hyperplasia.

Babies with CAH are born with a number of physical changes. Their adrenal glands are often larger than normal, even at birth. Girls with CAH may be born with external sex organs that appear more masculine than they should. If not treated, both boys and girls will develop early sexual characteristics, well before normal puberty should begin.

WHAT CAUSES CONGENITAL ADRENAL HYPERPLASIA?

Normally, the adrenal glands make a number of different hormones, including cortisol, aldosterone and androgens. Hormones are chemicals that send messages to other organs or tissues of the body, telling them to do specific things.

CAH occurs when a particular enzyme called 21-hydroxylase (21-OH) is missing or not working correctly. The job of this enzyme is to help make cortisol and aldosterone in the adrenal glands so they can be released when the body needs them.

One of the main jobs of cortisol is to keep the amount of glucose, the sugar used for energy by the body's cells, at a normal level. Cortisol also helps protect the body during times of physical or emotional stress such as surgery, injury or illness. It helps to regulate the immune response and inflammation so our bodies can deal with infection or illness.

Another hormone made by the adrenal glands is aldosterone. This hormone is released into the blood when the blood pressure drops too low. It tells the kidneys to pull salt and water out of urine and put it back into the blood. This raises blood pressure back to normal and prevents the body from losing too much fluid. Babies with a form of CAH called "salt- wasting" do not make enough aldosterone and they lose too much salt and water in their urine. They become dehydrated and their blood pressure drops too low. This can be life-threatening if not treated quickly.

The other hormones made by the adrenal glands are called androgens. These are male-like sex hormones. The adrenal glands also make a small amount of female hormones.

Most people with CAH make too much of the androgen hormones and not enough cortisol or aldosterone. Having too much of the androgen hormones in the blood causes female babies to develop masculine changes to their genitals. And, high levels of androgens lead to early sexual development, well before the normal age of puberty, in both boys and girls.

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IF CAH IS NOT TREATED, WHAT PROBLEMS OCCUR?

The effects of CAH can vary greatly from person to person. There are a number of different forms of CAH which are described below.

Most babies found to have CAH during newborn screening have 'classic CAH'. One type of classic CAH is called 'salt- wasting' which is a serious condition needing immediate treatment. The other type of classic CAH is called 'simple virilizing'. Children with this type do not have immediate risks to their health but still need treatment.

A small number of children are found through newborn screening to have milder or 'nonclassic CAH' which often causes fewer health problems. The symptoms of nonclassic CAH are quite variable from person to person.

Classic CAH – "Salt-wasting form"

About 75% of babies with classic CAH have the 'salt-wasting' form. Salt-wasting CAH occurs when the adrenal glands make lower amounts of both cortisol and aldosterone and too much androgen. Babies who do not make enough aldosterone will start losing too much water and salt in their urine. This can quickly cause dehydration and very low blood pressure. This can be life-threatening if not treated right away.

Infants with salt-wasting CAH usually show some of the following features within the first few weeks of life:

- Poor feeding
- Listlessness and drowsiness
- Vomiting
- Diarrhea
- Dehydration
- Weight loss
- Low blood pressure
- Low blood salt (low blood sodium level)
- Too much acid in the blood, called metabolic acidosis

If not treated, severe dehydration leads to shock, a serious situation in which not enough blood is getting to the brain and other organs. In babies with salt-wasting CAH, this is also called an "adrenal crisis". The signs of an adrenal crisis include:

- Confusion
- Irritability
- Rapid heart rate
- Coma

Periods of adrenal crisis due to too little aldosterone can occur as early as one week to one month of age. If a child in shock is not treated, there is a risk of death.

Even when carefully treated, children with salt-wasting CAH are still at risk for adrenal crises when they become ill or are under stress. The body needs more than the usual amount of adrenal hormones during illness, injury or stress. This means a child with CAH must be given more medication during these times to prevent an adrenal crisis.

All babies with salt-wasting CAH have the other features of classic CAH listed below. Girls with salt-wasting CAH usually have more male-like changes to their genitals than girls with simple virilizing CAH.

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Classic CAH – Simple virilizing form

About 25% of babies with CAH have the simple virilizing form. The adrenal glands make enough aldosterone but not enough cortisol; they also make too much androgen.

Classic CAH starts its effects before birth. Excess androgen hormones are made by the fetus. This causes the genitals of female fetuses to develop male-like features. Baby girls born with classic CAH often have an enlarged clitoris. In some girls this is not very noticeable, but in others it may look like a small penis. Baby girls may also have labia which are fused together, may be wrinkled and may look more like a male scrotum. Some baby girls have fewer genital changes than others. The high level of androgen hormones does not affect the uterus and ovaries, which develop normally.

Girls who are not treated may develop other male-like traits and behaviors as they grow. Some of these changes may include:

- Deep, husky voice
- Excess hair on the face and body
- Lack of menstrual periods or scanty or irregular periods
- Early puberty changes such as hair in the armpits and pubic area
- Severe acne
- Male-pattern baldness (loss of hair near the temples)

Boys who are not treated may have some of the following traits:

- Muscle growth at an early age
- Pubic hair and underarm hair during childhood
- Enlargement of the penis during childhood
- Early deepening of the voice
- Early beard
- Smaller than normal testicles
- Severe acne

Sometimes the changes of early puberty happen in boys and girls as young as two to four years old. Both boys and girls may have rapid growth during childhood but end up being short as adults. Excess androgen hormones in childhood cause the rapid growth. The androgens also cause shorter adult height by closing the growth plates too soon. Some untreated adults also have problems with infertility and may have diffculty achieving pregnancy.

Children with simple virilizing CAH are at risk for adrenal crises, though typically less severe than seen in children with the salt-wasting form. Acute illness or stress increases the body's need for cortisol. If children with CAH do not receive increased amounts of medication during illness or stress, they are at risk for health problems.

Nonclassic CAH / Late-onset CAH

Nonclassic CAH, also called 'late-onset', usually causes milder effects than classic CAH. However, symptoms can be quite variable from person to person. Many people with nonclassic CAH often start showing signs during childhood, adolescence, or early adulthood. Some people never develop symptoms. Newborn screening can detect some, though not all, babies with the nonclassic form of CAH.

Babies with nonclassic CAH are usually healthy at birth and their genitals are normal in appearance. They do not have salt- wasting and are not at risk for adrenal crises.

Children and adults with nonclassic CAH have adrenal glands that make near-normal amounts of cortisol and normal amounts of aldosterone. However, they have too much 17-OH progesterone (17-OHP), a chemical used to make cortisol, in their blood. They also may make too much of the androgen hormones.

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Some of the traits that are sometimes seen in both males and females with non-classic CAH include:

- Rapid growth in childhood and early teens with short adult height
- Severe acne
- Early puberty with development of pubic hair, underarm hair and body odor during childhood Excess hair on the face and other parts of the body
- Male-pattern baldness (hair loss near the temples)

Girls and women may have:

- Male-like changes in physical appearance and behavior
- Irregular menstrual periods or early-onset of periods
- Infertility
- Polycystic ovary syndrome

Boys may have:

- Early beard growth
- Enlarged penis
- Small testicles

WHAT IS THE TREATMENT OF CAH?

Your baby's primary doctor may work with a pediatric endocrinologist to provide medical care to your child. It is important for babies with classic CAH to be diagnosed as quickly as possible. This allows treatment to begin soon after birth which helps reduce the effects of CAH.

The main treatment for classic CAH is a drug called 'hydrocortisone' (also called 'cortisone'), taken in pill form. This medication replaces the cortisol that your baby cannot make on his or her own. It must be taken daily throughout life to prevent effects of CAH. Cortisone is sometimes given in other drug form, such as prednisone or dexamethasone.

TREATMENT FOR CLASSIC CAH – BOTH SIMPLE VIRILIZING AND SALT-WASTING FORMS:

Cortisone medication

The main treatment is to replace the amount of cortisol not being made by the adrenal glands. Hydrocortisone, a synthetic form of cortisol, is given by mouth in pill form. This treatment lessens the amount of androgens, prevents early puberty, and allows for more typical growth and development. Your doctor will follow your child's growth, pubertal development, blood pressure, and hormone levels throughout childhood. The level of medication needed to control symptoms will be adjusted as needed throughout your child's life.

It is important to always follow your doctor's orders on how much cortisone to give your child. Too much cortisone can cause temporary symptoms of Cushing syndrome so the dose must be carefully balanced to your child's height, weight and activity level. Signs of Cushing syndrome include: stretch marks on the skin, rounded face, weight gain, high blood pressure, and bone loss.

In addition, your doctor will give you instructions for increasing the dose of hydrocortisone during an acute illness. If you have questions about dosing, call your doctor. The body needs more cortisol during illness, injury or times of stress. Therefore, the cortisone dosage must be increased by your doctor when your child is ill, injured, or requires surgery. If your child is ill and cannot take the pills, cortisone injections may be necessary.

Hydrocortisone must be taken throughout life to prevent CAH effects. If the medication is stopped, symptoms will develop.

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Surgery for girls with classic CAH

Girls who are born with an enlarged clitoris or changes to the labia have the option of surgery to change their outer genitals to a more female appearance. Some women who have CAH have not had surgery and are happy they did not. Others are glad their parents decided to give them the surgery. This is a complex decision made by the parents with guidance from their doctors. Parents who are not sure about surgery may want to talk with other families who have faced similar decisions.

If you choose corrective surgery, it can be done as early as age one to three. Surgery on the clitoris usually hides the excess tissue but leaves the clitoris itself intact. Surgery to separate the labia and to create a normal vagina is often delayed until the teenage years. Ask your doctor about the risks and benefits of surgery for these changes and the best time to do these surgeries.

Treatment to prevent short stature

Your doctor may take periodic X-rays to check your child's 'bone age'. This allows your doctor to tell whether your child is growing at too rapid a rate. It also shows whether the growth plates are still open or whether they are closing too early.

Specific medications may help increase height in children and teens that show signs of early growth failure. Certain medications lower androgen levels. If you have questions about your child's growth, talk to your doctor about the costs and benefits of these treatments.

Treatment for early puberty

Children who show changes of puberty at a young age are sometimes treated with medications that lower the amount of androgen hormones. Your doctor will talk to you about these medications should your child start showing signs of puberty during childhood.

Additional treatment for classic CAH – salt-wasting form

Children with salt-wasting CAH need to take an additional medication called Florinef. Florinef (9a-fludrohydrocortisone) is a 'salt-retaining' drug that replaces the aldosterone absent in children with salt-wasting CAH. It is given by mouth in pill form.

Some children with salt-wasting CAH need to follow a food plan that contains more salt than usual. In addition, your doctor may recommend salt tablets to prevent dehydration. It is important to follow your doctor's instructions on how much salt to feed your child. Most children on medication do not need to add extra salt to their diets.

TREATMENT FOR NONCLASSIC CAH

Some people with nonclassic CAH do not need treatment and may go through life without symptoms. Others begin having symptoms in childhood, adolescence or young adulthood and may need medication in the form of cortisone pills. Symptoms that may signal the need for treatment include:

- Severe acne
- Excess body hair
- Irregular menstrual periods
- Lumps in the testicles
- Infertility

Children and adults with nonclassic CAH usually need less medication than children with classic CAH.

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What happens when CAH is treated?

Children with CAH who start treatment soon after birth usually have normal growth and development. In most treated children, puberty occurs at the normal age, although some still have early changes. Even when treated, some adults are shorter than average.

Girls on medication usually have normal menstrual periods. Pregnancy is possible, although fertility may be lessened in some women.

Children with salt-wasting CAH who remain on treatment usually do not have further salt-wasting adrenal crises or other associated health problems.

Pregnant women with classic salt-wasting CAH should be followed carefully by an endocrinologist during pregnancy. Medications may need to be increased during pregnancy to prevent problems with fetal growth.

What causes the 21-hydroxylase enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. People with CAH have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the 21-OH enzyme either does not work properly or is not made at all.

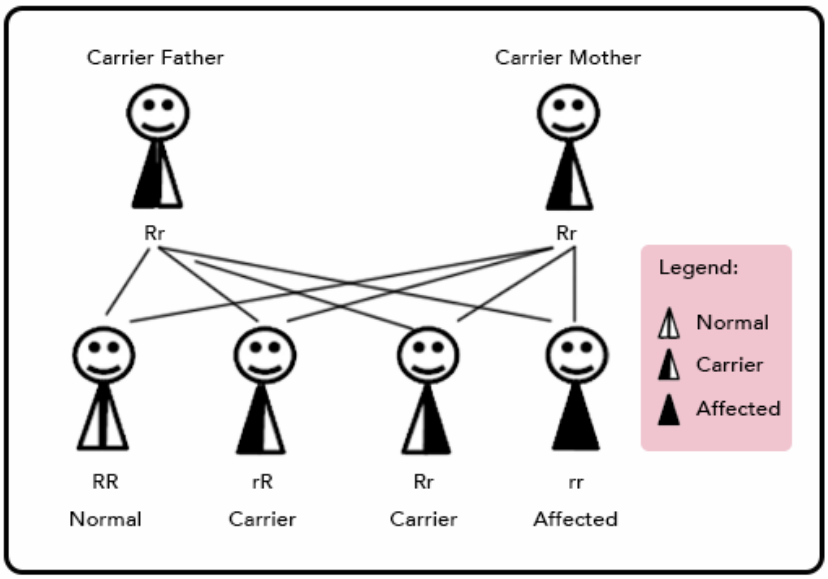
HOW IS CAH INHERITED?

CAH is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has a pair of genes that make the 21-OH enzyme. In children with CAH, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent.

Parents of children with CAH rarely have the condition themselves. Instead, each parent has a single non-working gene for CAH. They are called carriers. Carriers do not have CAH because the other gene of this pair is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have CAH. There is a 50% chance for the child to be a carrier, just like the parents. And, there is a 25% chance for the child to have two working genes.



Reference:

http://newbornscreening.info/Parents/otherdisorders/CAH.html
Accessed on 7 November 2014