CONGENITAL ADRENAL HYPERPLASIA

What is Congenital Adrenal Hyperplasia?

Congenital Adrenal Hyperplasia is a condition in which the **Adrenal Glands** produce excessive amounts of sex steroids and not enough of the other steroid hormones, which the body needs. This handout explains how and why this happens.

What are the Adrenal Glands?

The **Adrenal Glands** are small organs that are located just above the kidneys. They make several types of **hormones**, substances which the body needs in order to function normally. Hormones made by the adrenal glands are known as **Steroids**. The two most important steroids produced by the adrenal glands are called **CORTISOL** and **ALDOSTERONE**. The adrenal glands are the only place in the body where cortisol and aldosterone are made. The **normal** adrenal glands also produce **small** amounts of male hormones. The most important male hormone is testosterone, which is also produced in the testicles.

Cortisol is a steroid hormone which helps the body recover from stresses, such as illnesses and accidents. During these events, the body normally produces extra amounts of cortisol - this helps the blood pressure from falling too low and helps the blood sugar levels from falling.

Aldosterone helps the kidneys maintain normal levels of salt (sodium and potassium) and water.

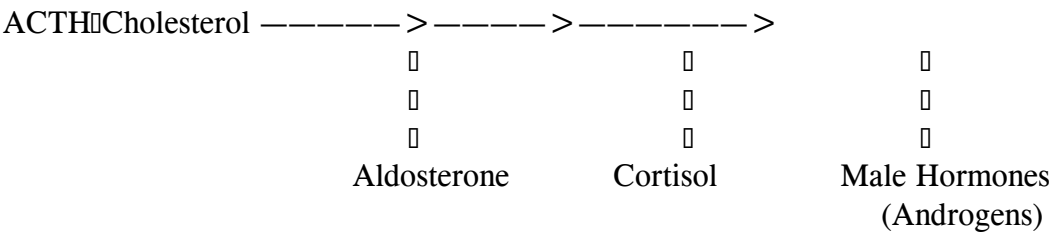
The small amounts of **testosterone** which are produced by **normal** adrenal glands help with the development of hair under the arms and around the genitals during puberty in both boys and girls. Adolescent boys produce much larger amounts of testosterone in the testicles, which accounts for most of the other body changes that occur in boys during puberty.

How do the Adrenal Glands produce steroid hormones?

In order to understand what happens in Congenital Adrenal Hyperplasia, it is important to know a little bit about how steroid hormones are produced.

The adrenal glands are like little factories that manufacture steroid hormones from cholesterol. The adrenal glands take up the cholesterol from the blood. Chemicals within the adrenal glands, called **ENZYMES**, change the cholesterol into the steroid hormones in a series of steps. A different enzyme is responsible for each step. Separate pathways are used to produce each of the 3 steroids (cortisol, aldosterone, and male hormones). The enzymes are like the workers in a car factory who add parts on to the car frame in order to produce different car models.

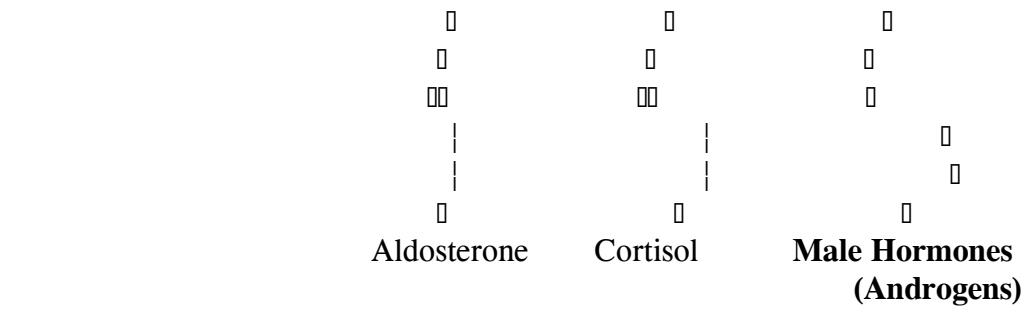
The pathways for the production of steroid hormones in the adrenal glands are shown in the picture below. Each arrow represents the actions of an enzyme.



Normal Adrenal Glands

What happens in Congenital Adrenal Hyperplasia?

In Congenital Adrenal Hyperplasia, a child is born with one of the enzymes missing, or present in only small amounts. The formal names for these enzymes are 21-hydroxylase and 11-hydroxylase. When one of these enzymes is missing or deficient, the adrenal glands cannot make adequate amounts of cortisol, and often cannot make enough aldosterone. The body senses the cortisol deficiency, and tries to stimulate the adrenal gland to take up more cholesterol from the blood. Since the adrenal glands cannot use all of this cholesterol to make cortisol and aldosterone, the metabolism of cholesterol is diverted to make unusually large amounts of male hormones. This situation is shown in the picture below, where an enzyme is missing in the pathways leading to cortisol and aldosterone production. The whole system backs up and starts producing excessive amounts of male hormones instead.



Congenital Adrenal Hyperplasia

The excessive concentrations of male hormones circulate in the bloodstream and cause the body to develop external male characteristics. In boys and girls, this can include genital enlargement, increased muscle growth, an adult-type body odor, increased body hair, oily hair, acne, and excessively rapid bone maturation. Children with Congenital Adrenal Hyperplasia can also develop a very tanned complexion, even without going out in the sun. The reasons for this are explained in the next section.

The cortisol deficiency decreases the body's ability to handle stresses such as major illnesses and accidents. If there is also an aldosterone deficiency, the body's salt balance can be abnormal, causing dangerously low sodium and high potassium levels. Children who have a severe enzyme deficiency can deteriorate much quicker following a stressful illness or accident, and they will have more male development than children, who have only a partial deficiency. Many children with severe enzyme deficiency will produce large amounts of male hormones even before they are born. If this happens to a female infant, she can be born with genitalia that appear almost like a boy. This is called **ambiguous genitalia**.

What causes the tanned complexion?

The adrenal glands are controlled by a portion of the brain called the **Pituitary Gland**. When the adrenal glands are not functioning properly, the pituitary gland senses this and produces large amounts of ACTH, a hormone that attempts to stimulate the adrenal glands to produce more cortisol. High levels of ACTH can also stimulate the pigment-producing cells in the skin [melanocytes], and the extra pigment gives the skin a tanned complexion. This tanned complexion will go away with proper treatment of the Congenital Adrenal Hyperplasia.

Why is the enzyme missing?

Children with Congenital Adrenal Hyperplasia are born with this condition, although, in some cases, this may not be diagnosed until many years after birth. This condition is inherited. Between 1% and 4% of all people carry the trait for Congenital Adrenal Hyperplasia. When two people who carry the trait marry and have children, the chances are about 1 in 4 that the child will inherit the trait from both parents. Children who inherit this "double-dose" develop Congenital Adrenal Hyperplasia. The prevalence of Congenital Adrenal Hyperplasia is approximately 1:7000 children. The precise frequency with which this occurs depends in part on the racial backgrounds of the parents, since some racial groups have an increased likelihood of carrying the trait. Because of this frequency, Congenital Adrenal Hyperplasia is now included in the newborn genetic screen that is performed on a heelstick blood sample obtained from all newborn babies [Athe PKU Screen@].

How is Congenital Adrenal Hyperplasia diagnosed?

Children who show excessive male development or abnormal salt balance, as described above, can have a blood test done to determine if they have Congenital Adrenal Hyperplasia. In this blood test, we determine the levels of the male hormone and the partially-formed or intermediate cortisol and aldosterone hormones. These levels are extremely high in Congenital Adrenal Hyperplasia. One of the partially-formed hormones that can build up in the blood is called **17-hydroxy-progesterone (17-OHP)**. Another hormone, called **RENIN**, is measured in order to determine salt balance. Both 17-OHP and Renin levels can be very high in untreated or inadequately treated Congenital Adrenal Hyperplasia.

Another test that is often ordered is called a **Bone Age X-ray**. This is an X-ray picture of one of the hands. From this picture, we can tell whether the male hormones have affected the maturation of the bones. If the bones mature unusually rapidly, your child could finish growing too soon and end up short. Treatment of the disease is designed to slow down this process and prevent the eventual short stature.

How is it treated?

Congenital Adrenal Hyperplasia is treated by replacing the missing Cortisol in the form of pills. When the body senses that the Cortisol levels are OK, the adrenal glands take up less cholesterol, and less male hormones are produced in the adrenal glands. Only a low dose of cortisol medication is required on a daily basis. During time of stress, however, extra amounts of cortisol are needed. This is described on the **EMERGENCY TREATMENT** sheet.

Children with Congenital Adrenal Hyperplasia are given a "short-acting" form of cortisol (**Cortef**, hydrocortisone) 2 or 3 times a day. Adults can be treated with a "long-acting" form (Prednisone or Dexamethasone) once a day. The long-acting form can interfere with normal childhood growth and development. When growth and development are complete, a long-acting form can then be used.

If Aldosterone is also missing, this is replaced with a pill called **Florinef**, which is given once or twice daily. The Florinef does not need to be increased during stress in most situations. Treatment of Congenital Adrenal Hyperplasia is monitored by regular physical examinations and blood tests. The doses of the medications often need to be adjusted as a child grows. Blood tests which may be checked include levels of Renin, 17-OHP, sodium, potassium, and male hormones.

A **bone age** X-ray is usually done approximately every other year to make sure that the bones are maturing at a normal pace. Your physician can explain these and other tests which may be obtained. Children with Congenital Adrenal Hyperplasia should visit a Pediatric Endocrinologist at least 4 times a year.

Because of the over-production of male hormones, girls who have Congenital Adrenal Hyperplasia, often have genitals that are somewhat male in appearance. If necessary, this can be corrected with surgery in combination with the medications described above. The surgery usually involves just the external genitals (clitoris, labia and vagina). The internal organs (uterus and ovaries) are usually normal. This will be explained in more detail if surgery is necessary for your child.

How is the dose of cortisol determined?

The daily amount of the cortisol (Cortef, hydrocortisone) medications which your physician has prescribed is about the same amount that would be produced by the adrenal glands if they were functioning properly. This is called the **physiologic dose** of cortisol. Your physician calculates this on the basis of body size (surface area) and laboratory testing.

During times of stress, extra amounts of cortisol medication are needed by the body (see the Emergency Treatment sheet). This is sometimes called the **pharmacologic dose** of cortisol. Pharmacologic doses of cortisol can be harmful if taken repeatedly or for a prolonged period of time (see next section). As a general guideline, **pharmacologic doses** of cortisol should not be given for more than 3 days in a row and the total time should not be more than 1 week each month unless recommended by your physician.

Will Congenital Adrenal Hyperplasia affect growth and development?

With proper treatment, children with Congenital Adrenal Hyperplasia have normal or near normal growth and development. Sometimes the excess amounts of male hormones that are produced before treatment begins can cause the bones to mature too rapidly. In this case, a child with Congenital Adrenal Hyperplasia may start out very tall for his or her age, but finish growing too soon. However, with early treatment, good compliance with taking medication, and with appropriate, frequent monitoring, most children with Congenital Adrenal Hyperplasia do reach a normal adult height.

UNDERtreatment (too little medication or lots of missed doses) will cause the adrenal glands to continue to produce large amounts of male hormones. This will cause excessive male body changes, and it will cause the bones to mature very rapidly and finish growing much too soon. Children who are UNDER treated may end up very short as adults. Girls who are UNDERtreated may develop male body features (lots of body hair, deep voice, acne, large clitoris, muscular build). Later in life, girls who are UNDERtreated may have very irregular menstrual periods or no periods at all. On the other hand, OVERtreatment with cortisol for a prolonged period can cause abnormal bone development (osteoporosis), high blood pressure, excessive body fat, and a number of other undesirable side effects. Therefore, it is very important for children with Congenital Adrenal Hyperplasia to visit their physician regularly in order to ensure proper

treatment.

Will it ever go away?

No. Children with Congenital Adrenal Hyperplasia are born with an enzyme deficiency - and this will not go away. Treatment will be required throughout life in order to make certain that the body is functioning normally, and that sexual development remains normal. It is fortunate that the treatment is relatively simple, and can be given with pills.

EMERGENCIES

When an individual with Congenital Adrenal Hyperplasia experiences physical stress, such as an illness or accident, the body will require extra amounts of cortisol in order to recover from the stress. Be sure that you are familiar with the emergency procedures listed on the Emergency Treatment sheet. Every person with Congenital Adrenal Hyperplasia should **ALWAYS** wear a bracelet or necklace (such as a **MEDIC-ALERT TAG**) so that in case of a severe emergency, medical personnel will know that extra cortisol is needed. The message on the tag should read:

Congenital Adrenal Hyperplasia - Takes hydrocortisone [and Florinef]

A wallet ID is **NOT** adequate since this may be lost during an emergency.

FINAL WORDS

Congenital Adrenal Hyperplasia is a life-long condition. It is important that you (and your child, if he or she is old enough) understand both the daily and emergency management of this disorder. You should know the names and doses for all of your child's medications, and your child should always wear an identification tag. With proper treatment, your child should lead a normal life without restrictions from school or sports activities. Regular visits to the physician will help ensure proper treatment and normal growth and development. If you have any questions, or if any emergencies arise, be sure to contact us or your family physician. The phone number for our office is **(303) 783-3883.**