Congenital Adrenal Hyperplasia (CAH)

Subdivisions of Congenital Adrenal Hyperplasia
11-Beta hydroxylase deficiency
17a-hydroxylase deficiency
21-hydroxylase deficiency
3-Beta-hydroxysteroid dehydrogenase deficiency
congenital lipoid adrenal hyperplasia
(this document focuses on the 21-hydroxylase deficiency)

A genetic disorder that affects the adrenal glands, a pair of walnut-sized organs above the kidneys. The genetic disorder causes that loss of the production of an enzyme that the adrenal glands use to produce hormones that regulate metabolism, the immune system, blood pressure and other essential functions. It affects 1 in 15000 children in the United States and Europe.

CAH affects the production of up to three steroid hormones:

1. Cortisol, which regulates the body's response to illness or stress.
2. Mineralocorticoids, such as aldosterone, which regulate sodium and potassium levels.
3. Androgens, such as testosterone, which are sex hormones.

In most cases, CAH results in lack of cortisol and overproduction of androgen.

The milder and more common form of CAH is called nonclassic. The classic form, which is more severe, can be detected in newborn screening programs. Some forms can cause problems with normal growth and development in children. There is no cure for CAH.

Symptoms of CAH vary, depending on which gene is defective and the level of enzyme deficiency.

Causes of CAH

CAH is passed along in an inheritance pattern called autosomal recessive. Children who have the condition have two parents who either have CAH or who are both carriers of the genetic mutation that causes the condition. Carriers of CAH show no symptoms.

In 95 percent of cases, the enzyme lacking in CAH is 21-hydroxylase. CAH may sometimes be called 21-hydroxylase deficiency. There are other and much rarer enzyme deficiencies that cause CAH.

Screening
Newborns are all screened for CAH when they are born. The screening process has a high false positive rate. According to one study 200 unaffected newborns required clinical and laboratory follow-up for every true case of CAH.

Classic CAH

Two-thirds of people with classic CAH are classified as having the salt-losing form, while one-third have the simple-virilizing form. Either one will produce genital ambiguity in females.

They may experience:

1. A lack of production of cortisol. Most problems are caused by lack of cortisol, which helps regulate blood pressure, maintain blood sugar and energy levels, and protecting against stress.

2. A lack of aldosterone (For salt-losing form). This can cause low blood pressure, a lower sodium level and a higher potassium level. Sodium and potassium help balance the fluids in the body.

3. Excess production of the male sex hormones (AKA: androgens, such as testosterone). This can cause short height, early puberty and in females abnormal genital development.

Signs and Symptoms (Infants):

1. In females, enlarged clitoris or genitals that look more male than female, which is called ambiguous genitalia, at birth. females still have normal internal female organs (ovaries and uterus).

2. Illness related to lack of cortisol, aldosterone or both, which is called an adrenal crisis.

Signs and Symptoms (Children/Adults):

1. Early pubic hair
2. Rapid growth during childhood, but shorter final height

Non-classic CAH

This is a milder form and often has no symptoms at birth. The form often only becomes evident in late childhood or early adulthood. They may only have deficiency in cortisol levels.

Signs and Symptoms (Females: teenage/adult):

1. Irregular or absent menstrual periods
2. Masculine characteristics such as facial hair, excessive body hair and a deepening voice
3. severe acne

Signs and Symptoms:

1. Early pubic hair
2. Rapid growth during childhood, but shorter final height

Complications

These depend on the type and severity of CAH.

People with classic CAH are at risk of experiencing adrenal crisis. This is caused by severely low levels of cortisol in the blood, resulting in diarrhea, vomiting, dehydration, low blood sugar levels and shock. It is a life-threatening medical emergency that requires immediate treatment. impaired production of aldosterone may occur as well, leading to dehydration with low sodium and high potassium levels. Adrenal crisis does not occur in the nonclassic form of CAH.

In classic and nonclassic CAH, males and females may eventually experience fertility problems.

Treatment

1. Supplying enough glucocorticoid to reduce hyperplasia and overproduction of androgens or mineralocorticoids.

2. Providing replacement mineralocorticoid and extra salt if the person isdeficient.

3. Providing replacement testosterone or estrogen at puberty if the person is deficient.

4. Additional treatments to optimize growth by delaying puberty or delaying bone maturation. Dexamethasone is used as an off-label early prenatal treatment for the symptoms of CAH in female fetuses, but does not treat the congenital disorder. It is still not fully clear how this affects females in every stage in life.

The dose of glucocorticoids should be minimized to avoid development of Cushing's syndrome, a disorder characterized by a variety of symptoms and physical abnormalities including weight gain; skin, muscle and bone changes. High dose mineralocorticoid supplements or salt should be avoided to prevent high blood pressure.

Medications

Dexamethasone

Called By: Decadron, Dexasone, and Diodex or Hedadrol

A corticosteroid hormone (glucocorticoid). It decreases your body's natural defensive response and reduces symptoms such as swelling and allergic-type reactions. Biological half-life is about 36-54 hours.

Can be 30 times more potent then hydrocortisone

Hydrocortisone

Called By: Cortef, Hydrocortone

A natural substance (corticosteroid hormone) made by the adrenal glands. It decreases the immune system's response to various diseases to reduce symptoms such as pain, swelling, and allergic-type reactions.

corticosteroids are needed in many ways for the body to function well. They are important for salt and water balance and keeping blood pressure normal.

Is the name for the hormone cortisol when supplied as medication.

Hydrocortisone is in a class of drugs called steroids. The biological half-life is about 100 minutes. Can also be refereed to as cortef, solu-cortef, and cortenema.

Prednisone

Called By: Deltasone

Prednisone is a synthetic corticosteroid drug. The elimination half life is about 3 to 4 hours, this is the time it takes for the body to reduce plasma levels by half. It takes about 5.5 half lives to be completely eliminated from the body.

Fludrocortisone

Called By: Florinef

Fludrocortisone is a class of drugs called steroids, so its a corticosteroid. Used to treat conditions in which the body does not produce enough of its own steroid. Also used along with hydrocortisone, prednisone, or dexamethasone to treat low glucocorticoid levels. It is used to help control the amount of sodium and fluids in your body. The plasma half-life is about 3.5 hours and a biological half-life about 18-36 hours.

Glossary

Adrenal Cortex - This is the outer portion of the adrenal gland. It produces steroid hormones that regulate carbohydrate and fat metabolism and mineralocorticoid hormones that regulate salt and water balance in the body.

Adrenal Glands (suprarenal glands) - These are endocrine glands that produce a variety of hormones including adrenaline and the steroids aldosterone and cortisol. They are found above the kidneys.

Aldosterone (a mineralocorticoid) - Helps keep a proper balance of salt (sodium) and water in the body that simulates absorption of sodium. Essentially, regulates blood volume and blood pressure.

Androgens (male sex hormone) - Control puberty, growth, and male sexual characteristics.

Biosynthesis - the production of complex molecules within living organisms or cells.

Corticosteroid - These are steroid hormones that are either produced by the adrenal cortex or made synthetically. There are two kinds: one is called glucocorticoids and the other is called mineralocorticoids.

Cortisol (a glucocorticoid) - Helps the body cope with stress, illness, and injury. Regulates blood glucose and blood pressure levels.

Cytochrome P450 enzyme - group of enzymes involved in drug metabolism and found in high levels in the liver. These enzymes change many drugs, including anticancer drugs, into less toxic forms that are easier for the body to excrete.

Enzymes - proteins that cause chemical changes in the body.

Estrogens (female sex hormones) - Control puberty, growth and female sexual characteristics.

Glucocorticoid - any of a group of corticosteroids, such as hydrocortisone, that are involved in the metabolism of carbohydrates, protiens, and fats and have anti-inflammatory activity.

Mineralocorticoid - a corticosteroid, such as aldosterone, that is involved with maintaining the salt balance of the body.

Virilization - the development of male physical characteristics, muscle bulk, body hair, and deep voice, in a female or earlier in a boy, typically as a result of excess androgen production.

21-hydroxylase - a cytochrome P450 enzyme that is involved with the biosynthesis of the steroid hormones aldosterone and cortisol. These syntheses take place in the adrenal cortex. Also called 21-monooxygenase, 21alpha-Hydroxylase, P450 21A2, and 21beta-Hydroxylase.

Resources

https://www.mayoclinic.org/diseases-conditions/congenital-adrenal-hyperplasia/symptoms-causes/syc-20355205
https://en.wikipedia.org/wiki/Congenital_adrenal_hyperplasia
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