Adrenal Insufficiency:

What is Adrenal Insufficiency?

Adrenal insufficiency, also known as Addison's disease, is a disorder characterized by the inability of the adrenal glands to produce an adequate amount of hormones, particularly cortisol and aldosterone. The adrenal glands, which are located on top of each kidney, and makes 3 types of hormones: corticosteroids or glucocorticoids (the main hormone is cortisol, which is also known as *hydrocortisone*); mineralocorticoids (the main hormone is aldosterone); and weak male-type sex steroid hormones known as the *adrenal androgens* which play a crucial role in producing hormones that regulate various bodily functions.

Cortisol is a hormone that helps to maintain blood sugar levels and helps in metabolism of fat, protein, and carbohydrates. Cortisol is especially important in times of stress. *Aldosterone* controls salt balance in the body through its effect on the kidney. *Adrenal androgens* are the hormones that are responsible for the development of pubic and underarm hair.

Production of cortisol by the adrenal gland is controlled by the pituitary gland hormone called *adrenocorticotropic hormone* (ACTH), which, in turn, is controlled by a brain hormone called *corticotropin-releasing hormone* (CRH).

There are two main types of adrenal insufficiency:

1. Primary adrenal insufficiency (Addison's disease): This occurs when the adrenal glands themselves are damaged and cannot produce enough cortisol and aldosterone. The most common cause of primary adrenal insufficiency is autoimmune destruction of the adrenal glands, where the body's immune system mistakenly attacks and damages the adrenal tissue. Other causes may include infections, certain medications, adrenal gland tumors, or genetic disorders.
2. Secondary adrenal insufficiency: This type occurs when the dysfunction is not in the adrenal glands themselves but rather in the pituitary gland or hypothalamus in the brain, which regulate the production of cortisol by signaling the adrenal glands. Causes of secondary adrenal insufficiency may include pituitary tumors, pituitary surgery, head trauma, or long-term use of corticosteroid medications that suppress the body's natural cortisol production.

What Are the Symptoms of Adrenal Insufficiency?

Symptoms of adrenal insufficiency can vary but may include fatigue, weakness, weight loss, low blood pressure, dizziness, salt cravings, nausea, vomiting, abdominal pain, darkening of the skin, and in severe cases, a life-threatening condition called an adrenal crisis, characterized by extremely low blood pressure and electrolyte imbalances.

Infants may fail to regain their birth weight and have trouble feeding.

What Causes Adrenal Insufficiency?

Adrenal insufficiency can be caused by various factors depending on whether it is primary or secondary adrenal insufficiency.

1. Primary Adrenal Insufficiency (Addison's Disease):
    - Autoimmune destruction: The most common cause of primary adrenal insufficiency is autoimmune destruction of the adrenal glands, where the body's immune system mistakenly attacks and damages the adrenal tissue.
    - Infections: Certain infections, such as tuberculosis or fungal infections, can affect the adrenal glands and lead to their dysfunction.
    - Genetic disorders: Rare genetic conditions, such as congenital adrenal hyperplasia or familial glucocorticoid deficiency, can cause adrenal insufficiency.
    - Adrenal gland disorders: Conditions such as adrenal gland tumors, adrenal hemorrhage (e.g., due to trauma or anticoagulant therapy), or adrenal gland surgery can impair adrenal function.
2. Secondary Adrenal Insufficiency:
    - Pituitary disorders: Damage or dysfunction of the pituitary gland, which produces adrenocorticotropic hormone (ACTH), can result in secondary adrenal insufficiency. This can be caused by pituitary tumors, pituitary surgery, head trauma, or radiation therapy to the pituitary gland.
    - Hypothalamic disorders: Dysfunction of the hypothalamus, which regulates the secretion of corticotropin-releasing hormone (CRH) that stimulates the pituitary to produce ACTH, can also lead to secondary adrenal insufficiency. Causes may include tumors, trauma, or radiation affecting the hypothalamus.

Additionally, certain medications can suppress the adrenal glands' function and lead to adrenal insufficiency, either by directly affecting adrenal hormone production or by inhibiting the release of ACTH from the pituitary gland. These medications include long-term use of corticosteroids (such as prednisone), which can suppress the body's natural cortisol production, as well as some drugs used in the treatment of Cushing's syndrome.

How is Adrenal Insufficiency Diagnosed?

Diagnosis of adrenal insufficiency typically involves blood tests to measure cortisol and aldosterone levels along with ACTH and renin, as well as stimulation tests (synacthen stimulation test) to assess the adrenal glands' response to hormone stimulation.

Imaging tests such as CT scans or MRI may also be performed to evaluate the adrenal glands and detect any structural abnormalities.

How is Adrenal Insufficiency Treated?

Treatment of adrenal insufficiency involves hormone replacement therapy to replace the deficient hormones. This usually includes oral corticosteroids (such as hydrocortisone) to replace cortisol and, if necessary, medications to replace aldosterone. Oral hydrocortisone or other similar medications are used to replace cortisol and need to be taken 2 to 3 times a day. Patients with aldosterone deficiency usually take a pill called fludrocortisone to help maintain salt balance.

Patients with adrenal insufficiency also need to be educated about the signs and symptoms of adrenal crisis and instructed on how to manage stress, illness, or injury to prevent crises.The hydrocortisone dose will usually need to be increased at times of significant body stress because your child’s body cannot make more hydrocortisone. This is called stress dosing.

Overall, with proper treatment and management, most people with adrenal insufficiency can lead normal lives, although lifelong hormone replacement therapy and regular medical monitoring are typically required.

Can Adrenal Insufficiency Crises be Prevented?

Once the diagnosis of adrenal insufficiency has been confirmed, parents and patients need to learn how and when to administer daily medication and the higher cortisol doses for stress situations. All patients should wear medical alert identification badges.

Congenital Adrenal Hyperplasia:

What is Congenital Adrenal Hyperplasia (CAH)?

Congenital adrenal hyperplasia (CAH) is a group of inherited genetic disorders characterized by the deficiency of enzymes involved in the production of cortisol and aldosterone in the adrenal glands. These enzymes are necessary for the synthesis of cortisol from cholesterol.

The most common form of CAH is caused by a deficiency of the enzyme 21-hydroxylase, which leads to decreased cortisol production and an overproduction of androgens (male sex hormones) and, in some cases, aldosterone. This overproduction of androgens can result in abnormal development of the external genitalia in females (virilization) and in males may cause early appearance of masculine traits. In addition to genital abnormalities, individuals with CAH may also experience symptoms such as excessive hair growth (hirsutism), acne, irregular menstrual periods, infertility, and in severe cases, adrenal crisis.

How Common is CAH?

In the general population, the most severe form of CAH (classic 21-hydroxylase deficiency) occurs in approximately 1 in 15,000 people. The milder non-classic form of CAH is more common and occurs in approximately 1 in 1,000 people. The different types of CAH are caused by differences in the specific *CYP21A2* gene defects.

How is CAH Diagnosed?

CAH is typically diagnosed through newborn screening programs or when symptoms become apparent in infancy or early childhood. Diagnosis involves blood tests to measure hormone levels and genetic testing to identify mutations in the genes responsible for CAH.

How is CAH Treated?

Treatment of CAH aims to replace deficient hormones and suppress the overproduction of androgens. This often involves lifelong hormone replacement therapy with glucocorticoids (such as hydrocortisone) to replace cortisol and, if necessary, mineralocorticoids (such as fludrocortisone) to replace aldosterone. Additional medications may be prescribed to control excess androgens and manage symptoms. Close monitoring by healthcare providers is essential to adjust treatment as needed and prevent complications.

With early diagnosis and appropriate treatment, individuals with CAH can lead normal, healthy lives. Management typically involves a multidisciplinary approach with input from pediatric endocrinologists, geneticists, pediatricians, and other specialists to ensure optimal care.

Can CAH be Prevented?

CAH cannot be prevented. In the past, an experimental medication was prescribed for pregnant women who were at risk for having a newborn girl with CAH to prevent the overgrowth of the clitoris and atypical external genital appearance. This experimental medication does not cure CAH. In addition, current information indicates that this treatment may have negative effects in later life and is no longer recommended.

Families concerned about their risk of having another child with CAH should discuss this concern with their child's endocrinologist in consultation with a genetic counselor.