Addison's disease

Summary

- Addison's disease is a progressive disorder where the adrenal glands are unable to produce sufficient hormones.
- Causes can include infection, damage, and an autoimmune response that prompts the immune system to attack and destroy the adrenal glands.
- Treatment includes steroid replacement therapy that must be managed for life.
- An Addisonian crisis can be fatal unless treated quickly and appropriately.

Addison's disease (chronic adrenal insufficiency) is a rare and progressive disorder that affects between one and six in every 100,000 people. It affects people of both sexes and all ages.

The human body has two adrenal glands, one on top of each kidney. These glands form part of the endocrine system, which works with the nervous system and the immune system to help the body cope with different events and stresses. Addison's disease is caused by the inability of the adrenal glands to make sufficient amounts of regulating hormones.

Adrenaline is the best known of the hormones that are secreted by the adrenal glands in the adrenal medulla (the central part of the gland). The adrenal cortex (the outer part) also produces important hormones, the corticosteroids. They include cortisol, aldosterone and supplementary sex hormones.

In a person with Addison's disease, only the adrenal cortex is affected. The person cannot produce enough glucocorticoid or cortisol and, occasionally, also fails to produce sufficient mineralocorticoid. Levels of aldosterone are nearly always low in people with Addison’s disease.

Causes of Addison's disease

Most cases of Addison's disease are caused by an autoimmune response that attacks and damages the adrenal glands over time.

Other causes include:

- infection
- cancer
- surgical removal of particular tumours in the adrenal or pituitary glands or the hypothalamus.

Symptoms of Addison's disease

The symptoms of Addison's disease can include any or all of the following:

- loss of appetite and weight
- nausea, vomiting or diarrhoea
- muscle weakness
- chronic, worsening fatigue
- low blood pressure
- salt cravings
- dehydration
- hypoglycaemia, or low blood sugar levels (especially in children)
- increased pigmentation of the skin, particularly around scars and bony areas

- irregular or no menstrual periods in women
- mood swings, mental confusion or loss of consciousness.

These symptoms can develop quickly (especially in children and teenagers), or progress slowly for 20 years or more. Many symptoms can mimic other diseases, so diagnosis can be delayed.

The hormone cortisol

Cortisol is produced by the outer layer of the adrenal gland, called the adrenal cortex. The quantities of cortisol released by the adrenal glands are closely monitored by the master gland of the endocrine system, the pituitary, which is located in the brain.

The workings of the pituitary are governed by another brain structure, the hypothalamus. When cortisol levels are too low, the pituitary secretes the stimulating hormone adrenocorticotropin (ACTH). On the other hand, high levels of cortisol cause the pituitary gland to decrease ACTH secretion, which slows cortisol production.

Cortisol plays many vital roles and is essential to many body functions because it:

- works with adrenaline to help the body manage physical and emotional stress
- converts protein into glucose to boost flagging blood sugar levels
- works in tandem with the hormone insulin to maintain constant blood sugar levels
- reduces inflammation
- helps the body maintain a constant blood pressure
- helps the workings of the immune system.

The hormone aldosterone

Aldosterone is a mineralocorticoid, also produced by the adrenal cortex. The amount of aldosterone in the body is monitored by the kidneys, which secrete hormones to increase or decrease aldosterone production. Aldosterone regulates electrolytes (such as sodium and potassium) in the blood. This helps to maintain blood pressure and heart function.

If too much sodium is excreted by the kidneys, a considerable amount of body fluid is also lost. This reduces blood volume and drops blood pressure. Too much or too little potassium can affect the way the heart functions.

Primary adrenal insufficiency

Addison's disease can occur gradually, and is defined when approximately 90 per cent of the adrenal gland(s) is damaged. This is known as primary adrenal insufficiency. Around seven out of 10 cases of Addison's disease are caused by an autoimmune response, where the body's own immune cells attack and destroy the adrenal glands. In some cases, other glands of the endocrine system are affected by an autoimmune response, in a condition called polyendocrine deficiency syndrome.

Polyendocrine deficiency syndrome

There are two types of primary adrenal insufficiency and both types tend to run in families. They are:

- **Type I** – is more common in children. Symptoms include underactive parathyroid, pernicious anaemia, recurring candida infections, chronic active hepatitis and slow sexual development.
- **Type II** – (Schmidt's syndrome) is more common in younger adults. Symptoms include underactive thyroid, type 1 diabetes and, less commonly, vitiligo (a skin condition).

Other conditions related to primary Addison's disease are:

- **Adrenomyeloneuropathy (AMN)** – which can occur in some adults. It affects the spine and is degenerative over time.
- **Adrenoleukodystrophy (ALD)** – occurs (rarely) in some children (one in 100,000), especially males. It can cause brain damage and can be fatal. Survivors often develop AMN.

Treatment for primary Addison's disease is with glucocorticoid and mineralocorticoid replacement for life.

Secondary adrenal insufficiency

Sometimes, Addison's disease is caused by the pituitary gland's inability to produce sufficient amounts of ACTH, which means the adrenal glands aren't prompted to secrete cortisol. This is known as secondary adrenal insufficiency.

Causes of secondary adrenal insufficiency may include:

- **Some medications** – inflammatory disorders such as rheumatoid arthritis and asthma are often treated with prolonged or high-dose steroids (glucocorticoid replacements). If the dose is suddenly stopped, or not reduced by appropriate tapering measures, the pituitary gland may respond by failing to produce enough ACTH. This situation can sometimes be reversed.
- **Cushing's disease** – a benign tumour of the pituitary gland that produces ACTH. This results in too much cortisol being produced. Treatment requires surgical removal of the tumour and, in some cases, removal of damaged adrenal gland(s).
- **Other causes** – infections, reduced blood flow, radiotherapy and some neurosurgery can damage the pituitary gland or hypothalamus, and decrease the ability to produce ACTH.

Treatment for secondary Addison's disease is with glucocorticoid replacement only.

Addisonian crisis

A sudden, acute worsening of symptoms is known as an Addisonian crisis. If untreated, an Addisonian crisis can be fatal.

It can be caused by:

- **extreme stress** – an accident, excessive heat or physical exertion
- **severe illness** – especially dehydration from vomiting or diarrhoea
- **sudden shock** – for example, the death of a significant person.

The symptoms of Addisonian crisis include:

- violent pain in the abdomen, back and legs
- nausea, vomiting or diarrhoea
- low blood pressure, low blood sugar, high potassium, low sodium and a rapid heart rate
- possible mental confusion and loss of consciousness.

Prompt emergency hospital treatment must be sought, including intravenous fluids, increased steroid medication and saline. Many people who suffer from Addison’s wear a medical alert bracelet or pendant with information and identification, and carry a hydrocortisone injectable for use in emergencies. They will still need hospitalisation and ongoing monitoring.

Diagnosis of Addison's disease

Diagnosis may involve:

- a complete detailed family history, with special attention to any other endocrine disorders
- biochemical tests, which measure cortisol levels before and after a challenge injection of synthetic ACTH, known as a 'short synacthen test'. Synacthen tests will indicate the person's baseline level of cortisol production and their response to an increased need for cortisol in the body. An person who suffers from Addison’s may show a flat or reduced response
- blood electrolyte and plasma renin tests, which will indicate if there is a need for mineralocorticoid replacement
- anti-adrenal antibody test – if the result is positive, primary Addison's disease is definitively diagnosed. However, even if these antibodies do not exist, the person may still have Addison's disease
- x-rays, ultrasounds and CAT scans of the abdominal region to check for visual signs of damage and the size of adrenal glands.

Treatment of Addison's disease

Treatment aims to boost or replace insufficient or absent steroid components. Glucocorticoid replacement is essential for people suffering from primary or secondary Addison’s, and must be taken for life.

Treatment should:

- be tailored to each person over the course of their life
- be altered, in consultation with a doctor, during illness or other stressful events
- allow for the different needs of children and young adults.

Where to get help

- Your doctor
- **Australian Addison's Disease Association** Tel. **0455 534 472**
- **Australian Pituitary Foundation** Tel. **1300 331 807**

This page has been produced in consultation with and approved by:

Australian Addisons Disease Association