

SECONDARY ADRENAL INSUFFICIENCY

THE FACTS YOU NEED TO KNOW

WHAT IS SECONDARY ADRENAL INSUFFICIENCY?

There are normally two adrenal glands, located one above each kidney. The adrenal glands are really two endocrine glands in one. The inner part produces epinephrine (also called adrenaline). The outer portion of the adrenal is called the cortex. It makes two important steroid hormones, cortisol and aldosterone.

CORTISOL mobilizes nutrients, modifies the body's response to inflammation, stimulates the liver to raise the blood sugar, and also helps to control the amount of water in the body.

ALDOSTERONE regulates salt and water levels which affects blood volume and blood pressure.

Cortisol production is regulated by another hormone, adrenocorticotrophic hormone (ACTH), made in the pituitary gland, which is located just below the brain. In most individuals, aldosterone production is not dependent on ACTH.

Primary adrenal insufficiency, also known as Addison's disease, is caused by the total or near total destruction of the adrenal glands and results in the severe deficiency of both cortisol and aldosterone.

Secondary adrenal insufficiency, in contrast, is due to the absence of the normal stimulation to the adrenal cortex from a lack of ACTH. This results in a partial or total deficiency of cortisol, but often a normal or near normal production of aldosterone.

WHAT CAUSES SECONDARY ADRENAL INSUFFICIENCY?

- The two major types of secondary adrenal insufficiency are:
- Diseases that cause a total absence of ACTH, resulting in destruction of either the hypothalamus or pituitary gland
 - pituitary tumors, craniopharyngiomas
 - surgery to remove a tumor
 - radiation therapy to the pituitary
 - cysts in the pituitary
 - some inflammatory diseases
- Diseases that cause a suppression of ACTH production

The most common cause of this type is the use of glucocorticoid medications to treat a large variety of illnesses. Glucocorticoids are steroid hormones that act like cortisol, and include:

- oral form: cortisone, hydrocortisone, prednisone, prednisolone, dexamethasone
- intravenous or intramuscular administration
- inhaled and topical “steroids”

All of these medications have an effect on ACTH because the pituitary is producing this hormone in response to the body’s need for cortisol. When the cells in the pituitary recognize any of these drugs, they sense that there is cortisol present and therefore produce less ACTH.

This ACTH suppression from glucocorticoid medication can be very temporary, prolonged, or permanent depending on the dose, potency and length of use of the medication. For example, a few days of prednisone will not produce a significant problem, but several weeks of prednisone at a dose of 10 mg will diminish the cortisol level and the ability to fight a stressful situation.

Recovery of the pituitary-adrenal response after use of a suppressive dose for more than one month will take about one month. Generally, this one for one recovery time is typical up to about 9 to 12 months, when recovery will often take up to a year or may not occur at all.

WHAT ARE THE SYMPTOMS OF SECONDARY ADRENAL INSUFFICIENCY?

The symptoms are related to the degree of cortisol deficiency, the underlying health of the individual, and the rate of reduction in cortisol level. The most common symptoms are:

1. severe fatigue
2. loss of appetite, weight loss
3. nausea, vomiting, and diarrhea
4. muscle weakness
5. irritability and depression

Since aldosterone is usually present, low blood pressure and muscle spasms are not as likely as they are in primary adrenal insufficiency.

If secondary adrenal insufficiency is anticipated (i.e., after pituitary surgery, or after stopping glucocorticoids after a prolonged use for asthma), appropriate treatment may prevent any symptoms. However, if it is not expected, there are likely to be progressive chronic symptoms that may be missed or ignored until a sudden event like a flu virus, an accident, or the need for surgery suddenly precipitates a dramatic change for the worse. This is an adrenal crisis and is a medical emergency.

HOW IS SECONDARY ADRENAL INSUFFICIENCY DIAGNOSED?

The most important tool is the patient’s medical history.

Complete removal of the pituitary or the hypothalamus results in ACTH deficiency, and diagnostic testing may not be needed.

Those with a history of partial surgery or any of the diseases that may cause ACTH deficiency, including prolonged glucocorticoid therapy, may benefit from diagnostic testing.

Routine blood tests are often normal. These include:

- Potassium levels, which are typically high in primary adrenal insufficiency, usually normal because aldosterone is usually preserved.
- Blood sugar, which may be low, but not always.
- Blood cell counts which are usually normal.

DIAGNOSTIC TESTING: The most definitive test is the low dose ACTH (Cortrosyn) stimulation test. Blood levels of ACTH and cortisol are taken before the Cortrosyn administration, and a repeat cortisol level is taken one hour later.

A blunted or absent response shows that the adrenal reserve is abnormal. A serious dilemma in the use of this test is that it will be affected by recent use of glucocorticoid medication and many drugs used for other diseases.

It reflects the current state of adrenal responsiveness but may be misleading as a predictor of future recovery. For example, if it is performed after prednisone has been discontinued after several months of use, it may be abnormal, but could be repeated several weeks later and show significant recovery.

HOW IS SECONDARY ADRENAL INSUFFICIENCY TREATED?

Cortisol deficiency is treated with replacement oral glucocorticoid medication. Hydrocortisone is usually used, but the synthetic steroid prednisone may be used. Unless aldosterone deficiency is present, mineralocorticoid treatment with fludrocortisone is usually not needed.

Prednisone can usually be given as a single morning pill because it is long lasting. If hydrocortisone is used, it is typically given in divided doses with most of the daily dose in the morning and one or more smaller dose(s) midday and/or later afternoon to mimic the normal blood levels in people with normal adrenal function.

Extra doses of glucocorticoids are given for stress, such as:

- **infection, fever, injury**
- **coverage for surgery**

If an individual is severely ill, cannot take oral medication, or is having a procedure or surgery, the glucocorticoids must be given intravenously, usually in the form of IV hydrocortisone.

Maintenance treatment doses are adjusted for each individual. Higher or lower doses may be needed depending on many factors, including:

- other illnesses & need for other hormone replacements,
- need for other medication,
- weight and clinical response.

The lowest doses that prevent adrenal insufficiency symptoms are best. Chronic overdosing will cause signs and symptoms of glucocorticoid excess (Cushingoid features).

Those with permanent secondary adrenal insufficiency need replacement for the rest of their lives. The management of those who have developed secondary adrenal insufficiency from prolonged use of steroid therapy presents a challenge, in the following ways:

- Once glucocorticoids have been tapered to below 5 mg of prednisone, dosing for stress such as illness or surgery is still needed until there is full recovery of adrenal reserve, typically using a guide of one month for each month that steroids had been used.
- The most difficult issue is that symptoms of adrenal insufficiency will be present during the tapering phase, because low levels of cortisol are the only trigger to the pituitary to stimulate the return of ACTH production and the restoration of normal pituitary-adrenal responsiveness.
- The longer high dose steroids were given for a disease like asthma, rheumatoid arthritis, polymyalgia rheumatica or inflammatory bowel disease, the more likely that individual will suffer from adrenal insufficiency symptoms on withdrawal of the steroids.

In addition, tapering off the steroids may cause a relapse of the disease that had been treated, causing a combination of disease symptoms overlapping with adrenal insufficiency symptoms. That is why it is very common for steroid tapers to be aborted, with a temporary return to therapeutic doses of glucocorticoids, followed by a slow attempt at tapering if the primary disease is in remission.

WHY SHOULD SECONDARY ADRENAL INSUFFICIENCY PATIENTS CONSULT AN ENDOCRINOLOGIST?

Endocrinologists are specialists in hormonal diseases, including adrenal and pituitary conditions that cause secondary adrenal insufficiency. An endocrinologist will have more training and experience in properly diagnosing and treating secondary adrenal insufficiency than most physicians.

In addition, most cases of permanent secondary adrenal insufficiency should be managed by an endocrinologist. In cases of steroid withdrawal for the treatment of medical conditions, endocrinologists often work with the primary physician or specialist in that disease to assess the recovery of pituitary-adrenal reserve and provide guidance about whether long-term glucocorticoid therapy is needed.

HOW NORMAL IS A SECONDARY ADRENAL INSUFFICIENCY PATIENT'S LIFE?

As long as proper glucocorticoid replacement is taken every day, a patient can have a normal life. Since other medical conditions are usually present along with the cortisol deficiency, the quality of life may be affected by these conditions. If secondary adrenal insufficiency is due to pituitary disease, other hormone therapies may be needed. When it is due to prolonged suppression from the use of steroids for a medical condition, relapse of that condition will have a significant impact on daily function.

Every adrenal insufficiency patient should wear an identification bracelet or necklace stating that he or she has the disorder to insure proper emergency treatment. An identification card outlining treatment is also suggested.

Living well and safely with adrenal insufficiency demands that patients be self-aware and learn to evaluate their bodies. NADF supplies tools and information specifically created to help patients with this task.



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The National Adrenal Diseases Foundation is a non-profit organization providing information, education and support to all persons affected by adrenal disease. For more information on joining NADF, or to find a support group in your area, contact:

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