



Untangling

the Effects of **High Cortisol** in
Patients With **Cushing's Disease**

What is Cushing's disease?

Cushing's disease is a hormonal condition caused by a tumor on the pituitary gland, which is located at the base of the brain. The tumor is responsible for the extra cortisol in your body.

The many roles of cortisol—the “stress hormone”

Cortisol is a naturally occurring steroid hormone that is produced by the adrenal glands on the kidneys. Cortisol affects many different functions in your body.

Helps to control

- Blood pressure
- Sleep/wake cycle

Helps to reduce

- Inflammation

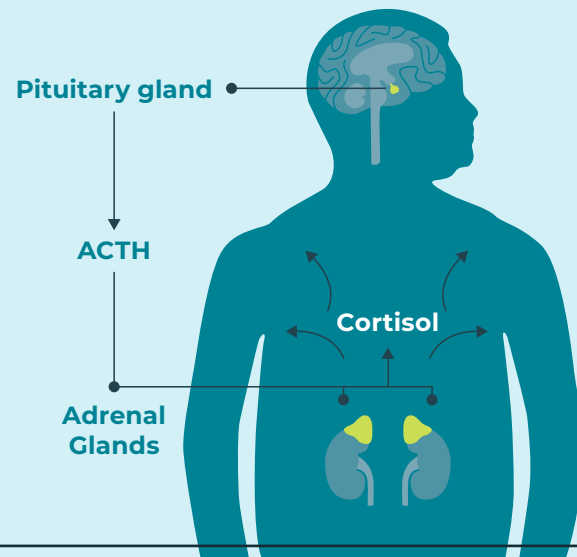
Helps to regulate

- Blood sugar levels
- Energy
- Stress response

The Cortisol Pathway

Regulating normal cortisol levels in the body

When the body needs cortisol, a pathway to release it begins in the pituitary gland, which is in the brain.



Cortisol is released via a specific pathway

1 The **pituitary gland**, when signaled by the brain, releases a hormone called **ACTH** (adrenocorticotropic hormone).

2 **ACTH** tells the adrenal glands on the kidneys to make and release cortisol.

3 **Cortisol** then binds to receptors in the body to function in its many roles. Normally, the brain senses when there is enough cortisol and tells the pituitary to slow the release of ACTH. This then signals the adrenal glands to stop making cortisol.

Causes of Hypercortisolism

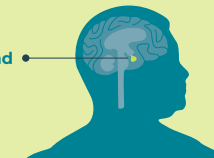
Hypercortisolism—elevated levels of cortisol

When left untreated for a long period of time, hypercortisolism can lead to the development of **Cushing's syndrome**. One subtype of Cushing's syndrome is called **Cushing's disease**, in which the source of extra cortisol in the body is specifically due to a tumor on the pituitary gland. Other types of Cushing's syndrome occur as a result of a tumor on the adrenal glands or elsewhere in the body, or due to steroid medications.

Pituitary gland tumor

Usually, a noncancerous (benign) tumor on the pituitary gland that interferes with the regulation of ACTH. This is referred to as **Cushing's disease**.

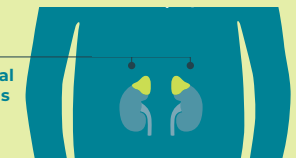
Pituitary gland



Adrenal gland tumor

Usually, a benign tumor on the adrenal glands that interferes with the regulation of cortisol. This may indicate a type of **Cushing's syndrome**.

Adrenal Glands



Ectopic tumor

Cushing's syndrome can also be caused by a tumor elsewhere in the body, known as an ectopic tumor.

Other

High cortisol can also be caused by factors outside the body such as steroid medications (known as corticosteroids), which act like cortisol. Some people take these medicines for asthma or arthritis.

Symptoms of Cushing's Syndrome and Disease

Diagnosing Cushing's Disease

Features of hypercortisolism in Cushing's disease

Over time, elevated cortisol levels can lead to many different physical and mental symptoms. **The first step in diagnosing Cushing's disease** is to identify patients who present with the signs and symptoms of hypercortisolism. These signs and symptoms may be different for each person.



Finding the source

To make sure patients receive the treatment that is right for them, additional tests are needed to determine the cause of excess cortisol.



After ruling out common causes for your symptoms (including any steroid medications), your healthcare provider may decide to test for Cushing's syndrome by measuring your cortisol levels.^a



No one test is perfect, so several tests may be conducted to accurately measure cortisol levels. Because cortisol levels change throughout the day, many of these tests involve overnight or all-day testing.



If high levels of cortisol are found, then the next step is to determine the source of the problem so that it can be treated. If the cause of high cortisol is from a pituitary tumor, then the diagnosis is Cushing's disease.

^aRandom testing of cortisol may not provide accurate results, and may lead to a delayed diagnosis or misdiagnosis. Testing your ACTH level may be used to help decide if you have Cushing's disease or Cushing's syndrome.

Testing

Screening tests for hypercortisolism

The next step in diagnosing Cushing's disease is to test for high levels of cortisol.

Late-night salivary cortisol

What it measures: Cortisol levels in saliva in the late evening. High cortisol may suggest Cushing's syndrome.

What to expect: Saliva is collected at bedtime by spitting in a plastic tube or by chewing on a piece of cotton to be returned to a healthcare professional in the morning.

24-hour urinary free cortisol (UFC)

What it measures: Cortisol levels in urine over a 24-hour period. Higher than normal cortisol levels detected in urine may suggest Cushing's syndrome.

What to expect: Urine is collected for 24 hours in a container and stored in a refrigerator until all is collected.

Low-dose dexamethasone suppression test (DST)

What it measures: How effectively your body manages the hormones ACTH and cortisol. Typically, after taking a dexamethasone tablet (a type of steroid), these hormone levels should decrease. If they remain high after the tablet, it might indicate Cushing's syndrome.

What to expect: 1 mg of dexamethasone is taken as a pill around bedtime. A healthcare professional will draw blood the following morning, usually around 8 AM.

Is your hypercortisolism due to elevated ACTH?

ACTH level testing

Once hypercortisolism has been confirmed, your doctor will measure your ACTH blood levels. If high levels of ACTH are causing the hypercortisolism, this may indicate Cushing's disease.

Testing for a pituitary tumor, which may indicate Cushing's disease

Magnetic resonance imaging (MRI)

What it detects: Possible presence, location, and size of a tumor.

What to expect: An MRI scan of your body to detect any tumors responsible for excess cortisol. During an MRI, the patient lies on a table that slides inside a tunnel-shaped machine.

Important to note: Many tumors, especially pituitary tumors, may be hard to detect because of their small size or location.

Bilateral inferior petrosal sinus sampling

What it measures: ACTH levels in the inferior petrosal sinuses (the sinus behind the nose) to detect presence of a pituitary tumor.

What to expect: After an injection of corticotropin-releasing hormone (CRH) (the hormone that causes the pituitary to release ACTH), samples of blood are taken from the petrosal sinus (veins from the pituitary gland in the brain). A second blood sample will be taken further away from the pituitary gland. Both samples will be compared. Higher levels of ACTH in the blood from the petrosal sinus may indicate a pituitary tumor. Similar ACTH levels in both samples may indicate a tumor elsewhere.

These are the most common tests used to diagnose Cushing's disease, but your healthcare provider may recommend other tests as well. This information is not meant to substitute the advice provided by a healthcare provider. Always consult a physician if you have health concerns.

Treatment Options for Cushing's Disease

Normalizing cortisol

After your screening and imaging tests confirm that Cushing's disease is the cause of your high cortisol, it's important to talk to your doctor about your treatment options. **The main goal of treatment for Cushing's disease is to normalize cortisol levels.** There are surgeries and medications that can help you achieve this goal. By talking to your doctor, you can decide which option is best for you.



Surgery

The first step to treating Cushing's disease is surgery to remove a tumor that has been detected. Removing the tumor can be a cure and may help the cortisol pathway return to normal, although it may take some time to feel better.



Medical Management

Though surgery is the first-line treatment, medical therapy may be an option for patients who have recurrent disease after surgery, or for those who cannot have surgery.



Radiation

If the tumor cannot be fully removed by surgery, radiation may help to control its growth. This may help lower cortisol levels, although it can take a long time. Medications will be needed while you wait for the radiation to work.

You Can

Resources—Take control with knowledge

Life with Cushing's Disease
cushingsdisease.com

Pituitary Network Association
pituitary.org

Hormone Health Network
admin.hormone.org

National Adrenal Diseases
Foundation
nadf.us

Cushing's Support &
Research Foundation
csrf.net

Pituitary World News
pituitaryworldnews.org

National Organization for
Rare Disorders
rarediseases.org