UNDERSTANDING
CUSHING'S DISEASE

What You
Need to Know

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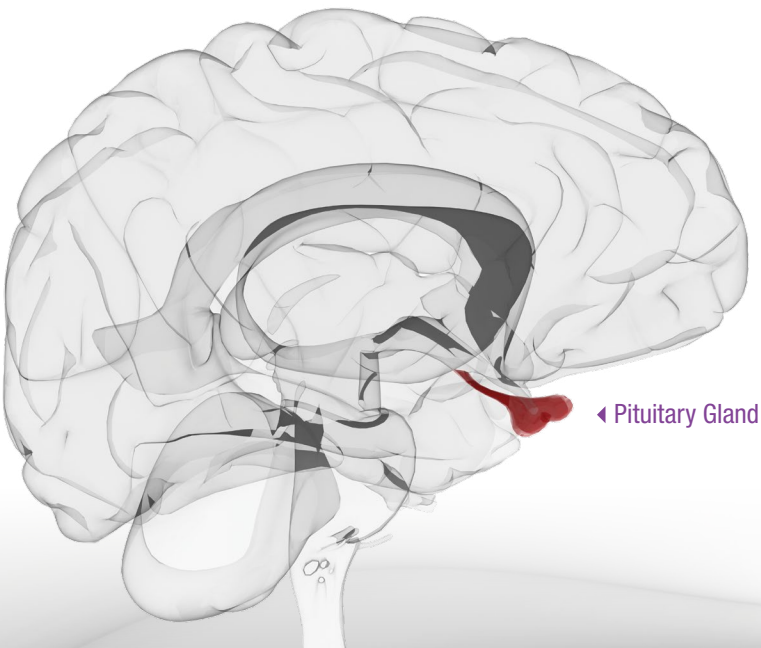
INTRODUCTION

By now you know you have been diagnosed with Cushing's disease. This rare condition is caused by a noncancerous tumor on the pituitary gland that is located at the base of the brain. The tumor causes the pituitary gland to release too much adrenocorticotropic hormone (ACTH). ACTH causes the production and release of cortisol, the stress hormone. Having too much ACTH leads to excess amounts of cortisol in the body, which may lead to a number of health issues.[1,2]

For many people with Cushing's disease, surgery to remove the tumor is the first step in treatment.[2,3]

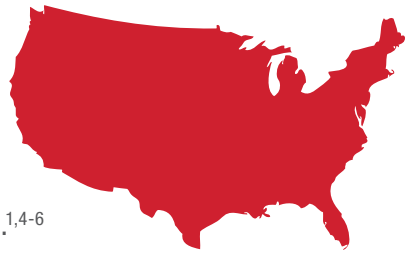
However, some people cannot or do not want to have surgery. And even for those who choose this option, surgery does not always achieve the desired or lasting results. For those individuals, drug therapy may be an appropriate choice.[2,3]

See the section called "Treating Cushing's Disease" on page 6 of this brochure to learn more about surgery as a treatment.



Cushing's Disease Is a Rare Disease

Cushing's disease affects an estimated 13,160 people in the United States.* It usually affects adults between the ages of 20 and 50, with women making up as many as 70% of cases.[1,4-6]



*Calculated based on estimated US population in 2020.

Caused by Excessive Levels of Cortisol

Under normal circumstances, cortisol is released in stressful situations. Cortisol also helps the body maintain normal blood pressure and cardiovascular function, and plays an important role in how the body uses carbohydrates, fats, and proteins.[2,7]

Cushing's disease is a condition in which excessive levels of cortisol are present in the blood. Cushing's disease results when a type of benign or noncancerous tumor called an adenoma develops on the pituitary gland in the brain and causes it to release excess amounts of ACTH.[1]

High levels of ACTH cause two small glands located on the top of the kidneys, called the adrenal glands, to release excessive levels of cortisol.[1]

Symptoms of Cushing's Disease

The symptoms of Cushing's disease are related to excess cortisol and may include[2]:

Changes in the physical appearance of the body

- Weight gain/obesity in the abdominal area with thin arms and legs
- Muscle weakness that can reduce the amount of time you are able to exercise
- Added fat on the back of the neck
- Rounding of the face
- Thinning and easy bruising of the skin
- Purplish stretch marks on the abdomen (abdominal striae)
- Reddening of the cheeks
- Excess hair growth on the face, neck, chest, abdomen, and thighs in women

General or systemic changes

- Weakness and fatigue
- Menstrual disorders
- Decreased sex drive and/or erectile dysfunction
- High blood pressure
- Type 2 diabetes mellitus
- Depression, anxiety, or changes in behavior

Diagnosing Cushing's Disease

The road to diagnosing Cushing's disease can be long, hard, and frustrating.[3] The symptoms of Cushing's disease are easily confused with the symptoms of other conditions, such as weight gain and high blood pressure, that are common in the general population.[8] And, because the changes in the body that occur with Cushing's disease may develop slowly at first, it may be difficult to diagnose Cushing's disease in the early stages.[8] In addition, hormone levels may decrease and rise again, making it even harder to reach a diagnosis.[3]

Initial diagnostic testing may include urinary free cortisol testing, late-night salivary cortisol testing, an overnight dexamethasone suppression test, and/or a 48-hour dexamethasone suppression test.[8]

A diagnosis of Cushing's disease will be confirmed if initial testing suggests a pituitary tumor and an MRI scan (magnetic resonance imaging) confirms the presence of such a tumor.[7]

Treating Cushing's Disease

Treatment options for Cushing's disease include surgery, radiation, and medication.[3] The first choice is surgery to remove the tumor. In people with small tumors, cure rates can be as high as 90%. If the first surgery produces an inadequate response, some people may have a second surgery and might have radiation therapy if the second surgery also produces an inadequate response.[3] But not all patients can or want to undergo surgery, and some patients do not achieve adequate disease control after surgery. For these patients, treatment with medication may be an appropriate option.

Regardless of the treatment plan you and your doctor decide is best, it is important to keep an open line of communication to help manage your treatment progress.

Committed to Advancing the Treatment of Rare Diseases

In the US, a rare disease is defined as a condition that affects fewer than 200,000 people.[9]

Recordati is committed to the research and development of treatments for rare diseases and is one of the most active companies in the field.[10]

While research and development efforts continue, Recordati Rare Diseases is here today to help patients and their physicians meet the challenges of diseases that have a significant impact on people's lives despite the small numbers of people those diseases affect. The company is **dedicated to partnering, discovering, and developing innovative products that improve the quality of life** and help people to enjoy longer, healthier, and more productive lives.[10]

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Resources for Additional Information

- JAMA Patient Page
- Merck Manual for Patients and Caregivers
- NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases)
- NORD (National Organization for Rare Disorders)
- Endocrine Society

References: 1. Genetics Home Reference. US National Library of Medicine. Cushing disease. https://ghr.nlm.nih.gov/condition/cushing-disease. Updated January 7, 2020. Accessed January 11, 2020. **2.** National Institutes of Health. US National Library of Medicine. Cushing disease. https://medlineplus.gov/ency/article/000348.htm. Updated January 6, 2020. Accessed January 11, 2020. **3.** Fish S, Findling J, Young W, eds. Hormone Health Network. Endocrine Society. Cushing's disease. https://www.hormone.org/diseases-and-conditions/cushings-disease. Updated October 2019. Accessed January 20, 2020. **4.** Etxabe J, Vazquez JA. Morbidity and mortality in Cushing's disease: an epidemiological approach. *Clin Endocrinol (Oxf).* 1994;40(4):479-484. **5.** US Census Bureau. US population clock. https://www.census.gov/popclock/. Updated February 12, 2020. Accessed February 12, 2020. **6.** Broder MS, Neary MP, Chang E, et al. Incidence of Cushing's syndrome and Cushing's disease in commercially-insured patients <65 years old in the United States. *Pituitary.* 2015;18(3):283. **7.** National Institutes of Health. US National Library of Medicine. Cushing's syndrome. https://www.niddk.nih.gov/-/media/Files/Endocrine-Diseases/Cushings_Syndrome_508.pdf. Updated July 2008. Accessed February 13, 2020. **8.** Nieman LK, Biller BM, Findling JW, et al. The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2008;93(5):1526-1540. **9.** US Food and Drug Administration. Developing products for rare diseases & conditions. https://www.fda.gov/industry/developing-products-rare-diseases-conditions. Updated December 20, 2018. Accessed January 11, 2020. **10.** Recordati Rare Diseases. Rare diseases and orphan drugs. Recordatirarediseases.com. Accessed January 11, 2020.

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