



The Hormone Foundation's

Patient Guide to the

Diagnosis of Cushing's Syndrome

Why were the Guidelines written?

This patient guide is based on Clinical Guidelines written to help physicians diagnose Cushing's syndrome (CS). CS is a condition that results when you have too much of the hormone cortisol in your bloodstream for a prolonged period of time. This can have harmful effects on muscles, bones, weight, heart, blood vessels, and the body's ability to fight infection.

There are two causes of CS—internal and external. External CS is more common. It is caused by taking medication containing *glucocorticoids* (cortisol-like medications) such as cortisone and prednisone. External CS goes away after you stop taking those medications. Internal CS affects an estimated 2 or 3 persons per million each year. It is caused by the body's over-production of the hormone cortisol.

Few, if any, signs and symptoms of CS are unique, and so diagnosis can be difficult, particularly in mild cases. This guide focuses on diagnostic tests that measure levels of cortisol in your urine, saliva, or blood.

How were the Guidelines developed?

The Clinical Guidelines were developed after an extensive review of the best human research studies related to the diagnosis of CS. An expert panel of The Endocrine Society examined studies that were published in "peer-reviewed" medical journals (that is, studies that were evaluated by other scientists). The panel then rated the quality of the studies.

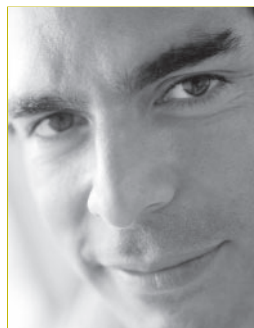
Once the panelists reached an agreement about their "recommendations" and "suggestions," the Guidelines were reviewed by the general membership of The Endocrine Society and approved by several of the Society's committees. No funding for the guidelines came from any pharmaceutical or medical device company.

Who should be tested for CS?

Before testing a patient who may have CS, the Clinical Guidelines recommend that physicians first ask about medications. This is to learn if the patient has recently taken glucocorticoids in any form—oral, rectal, inhaled, topical, or injected. It is important to know that skin creams (including bleaching agents), herbal medications, "tonics," and joint or nerve injections may include glucocorticoids.

Testing for internal CS is not necessary for patients who have received cortisol-like medications. In others, the Guidelines recommend testing for CS in the following patients:

- Patients with unusual signs and symptoms for their age. Examples are osteoporosis (brittle bones), high blood pressure, diabetes, or thin skin in younger patients.



If you think you have one or more signs of CS that would make you a good candidate for testing, talk with your doctor.

- Patients with several and worsening signs and symptoms that suggest CS. Examples of these features are easy bruising, swelling in the legs, facial redness, muscle loss and weakness, reddish-purple stretch marks, a rounded face, extra fat on the upper back and above the collarbone, and weight gain—especially around the belly.
- Children with poor height growth and increasing weight.
- Patients with a mass on the adrenal gland (the gland that produces cortisol). This is usually discovered coincidentally when diagnostic imaging such as a CT scan is used to analyze unrelated symptoms. A mass on the adrenal gland usually does not cause any problems, but some do produce extra cortisol.



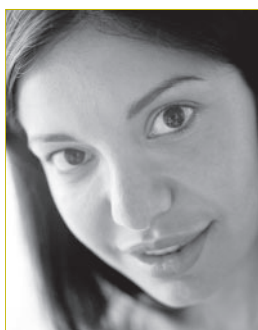
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What are the recommended diagnostic tests and how do you prepare for them?

The four recommended diagnostic tests measure whether there is too much cortisol in the urine, saliva, or blood:

Urine free cortisol (UFC) (at least two measurements should be done). This test measures the amount of cortisol in the urine over a 24-hour period. The urine cortisol is not affected by medications that alter the total cortisol measured in blood. For example, healthy women taking estrogen pills may have a high concentration of cortisol in their blood, but their UFC remains normal.

How you can prepare for this test: You shouldn't drink excessive amounts of fluids or use any glucocorticoid medications, including steroid-containing skin or hemorrhoid creams, over the 24-hour period when you are collecting your urine.



You and your doctor should be partners in your care. Discuss questions about diagnosis and treatment options.

Late-night salivary cortisol (2 measurements should be done). This test measures cortisol in the saliva late at night. In healthy people who go to sleep between 10 p.m. and midnight, the level of cortisol in the blood begins to rise at 3:00–4:00 a.m. and is highest at 7:00–9:00 a.m. It then falls for the rest of the day to very low levels at bedtime.

How you can prepare for this test: Several factors can increase the salivary cortisol result. Examples of these include extreme stress or excitement, and the use of licorice, cigarettes or chewing tobacco. You should avoid these activities on the day that you collect saliva. The timing of the collection should be adjusted to the time of sleeping if your bedtime is usually long after midnight.

1-mg overnight dexamethasone suppression test (DST). This test attempts to decrease the production of cortisol by means of the glucocorticoid dexamethasone. For the overnight test, you take 1 mg of dexamethasone between 11:00 p.m. and midnight, and then you have blood drawn between 8:00 and 9:00 a.m. the following morning to measure the cortisol level. In people who don't have CS, the 1-mg dose will greatly lower the blood cortisol level. In patients with internal CS, it won't.

How you can prepare for this test: You shouldn't eat or drink anything for 10–12 hours before the morning blood test.

Longer DST (2 mg/day for 48 hours). For this longer DST, dexamethasone is given in doses of 0.5 mg for 48 hours at 6-hour intervals. You take the first dose at 9:00 a.m. on day 1, the second at 3:00 p.m., the third at 9:00 p.m., and the

fourth at 3:00 a.m. The same is done on day two. On day three, blood is drawn at 9:00 a.m., 6 hours after the last dose of dexamethasone. The 2-mg 48-hour test better distinguishes CS from other conditions that can raise cortisol levels (such as depression, anxiety, obsessive compulsive disorder, extreme obesity, alcoholism, and diabetes).

How you can prepare for this test: It is very important to take the dexamethasone tablets at the correct times and not to miss any doses.

If your test results show that CS is unlikely, the Guidelines suggest re-evaluation in 6 months if your signs or symptoms progress. If you have at least one test result that indicates CS, they recommend further evaluation by an endocrinologist to confirm the diagnosis.

Are there special considerations in choosing a diagnostic test?

Several factors influence the choice of the best initial test. For pregnant women, the Guidelines recommend **for** the use of the UFC and **against** the use of the DST. For patients receiving medications used for seizure disorders, (such as phenytoin, phenobarbitone, and carbamazepine), the Guidelines recommend **against** the use of dexamethasone, which might give false positive results. Instead, they recommend measurements of UFC or late-night blood or salivary cortisol. For patients with kidney failure, the Guidelines suggest using the 1-mg overnight DST rather than UFC. In patients suspected of having mild CS due to an adrenal mass, the Guidelines suggest use of the 1-mg DST or late-night salivary cortisol test rather than UFC.

What can you do to help your testing?

You and your doctor should be partners in this process. Make sure to tell your doctor about all of the medications, supplements, creams, lotions, etc. that you have used in the last month, and whether you have had any injections in the last six months. This will help to identify possible external CS and also determine if you are taking drugs that may interfere with the diagnostic tests. For example, you may need to stop taking estrogen-containing drugs for six weeks before testing.

To ensure the best results, very carefully follow the instructions for collecting, storing, and submitting saliva or urine samples and for taking dexamethasone.

Many types of doctors perform the initial testing for CS. However, if your test results suggest CS, you should consult an endocrinologist (an expert in hormone-related conditions) about your diagnosis and treatment.

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May 2008