

Cortisol

MDL Test Number: 641

Methodology: Immunoassay

CPT Codes: 82533 x 1



Specimen Collection Platform:

Serum in Serum Separator Tube (SST)

Turnaround Time:

24 - 72 hours

Stability:

Room temperature

Test Additions*:

30 days to add tests

Specimen Collection:



1. Immediately after blood collection, invert the tube(s) gently 5 times to ensure mixing of clot activator.



2. Allow the tube to rest upright for at least 30 minutes after collection to ensure proper clotting.



3. Centrifuge for at least 15 minutes at 2200-2500 RPM within one hour of collection.



4. Do not remove the stopper or pour off serum.



What is Cortisol?

Cortisol is a steroid hormone made by the adrenal glands, two small glands that sit on top of the kidneys. It is the body's main stress hormone. It helps keep blood sugar and blood pressure steady, controls inflammation, and helps the body cope with illness and injury. How much is released is directed by the pituitary gland at the base of the brain, through a signal called ACTH.

Cortisol is not steady throughout the day. It peaks shortly after waking, falls through the afternoon, and reaches its lowest point late at night, so the same number can be normal in the morning and unexpected in the evening. It also climbs sharply with physical or emotional stress. Most of the cortisol in blood is carried on a protein, and only the small unattached portion is active. Anything that changes how much of that carrier protein is present — pregnancy, estrogen therapy, or serious illness — shifts the total without changing the active hormone. That is why both the time of the draw and the patient's medication list matter for this test.

Why test for Cortisol?

A healthcare provider may order a cortisol test to see how well the adrenal glands are working, or to look for too much or too little of the hormone. Common reasons include:

- **Telling polycystic ovary syndrome, also called polyendocrine metabolic ovarian syndrome (PMOS/PCOS), apart from Cushing syndrome.** Irregular periods, unwanted hair growth, weight gain, and acne occur in both, and cortisol is one of the tests that separates them.
- **Investigating suspected Cushing syndrome,** the condition caused by long-term cortisol excess. Other features include easy bruising, purple stretch marks, muscle weakness, and high blood pressure.
- **Looking into possible adrenal insufficiency,** where the glands do not make enough cortisol. Symptoms include lasting fatigue, weight loss, low blood pressure, salt craving, and darkening of the skin.
- **Evaluating a woman who could not breastfeed, or whose periods did not return, after a delivery complicated by heavy bleeding** — a pattern that can point to Sheehan syndrome.
- **Measuring the samples drawn during an ACTH stimulation or dexamethasone suppression protocol,** which is how most adrenal diagnoses are confirmed.
- **Checking adrenal function in a patient who has been on long-term steroid treatment and is coming off it.**



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Special Instructions:

- **Collection timing:** Draw the baseline sample in the morning, ideally between 7am and 9 am, when cortisol is at its daily peak. Record the actual time of the draw on the requisition; without it, the result cannot be placed against the right expected range.
- **Steroid medications:** Prednisone and prednisolone are close enough in structure to cortisol that the test reads them as cortisol and returns a falsely high result, and methylprednisolone does the same to a lesser degree. Dexamethasone does not interfere, which is why it is the steroid used in suppression testing. List every steroid the patient takes, including creams, inhalers, and joint injections.
- **Estrogen therapy and hormonal contraceptives:** Estrogen raises the carrier protein that cortisol travels on, so total cortisol reads high in women who are pregnant or taking estrogen, even when the active hormone is normal. Note pregnancy and any estrogen-containing medication, including combined pills, patches, and rings.
- **Recent stress or illness:** Cortisol rises with acute infection, injury, severe pain, and emotional stress. Where the question allows it, draw when the patient is well and settled, and note any current illness on the requisition.
- **Biotin supplements:** Biotin (vitamin B7) is found in many over-the-counter hair, skin, and nail supplements, and at high enough levels it can interfere with this test. The manufacturer has not published how long a patient should stop it before the draw, so patients should disclose biotin use and let the ordering provider decide on timing.
- **Comparing results over time:** Different laboratories and instruments can produce somewhat different cortisol numbers from the same sample, so results tracked over time should use the same test at the same laboratory. Samples drawn as a set during a stimulation or suppression protocol should all be run by the same method.

Limitations:

Every laboratory test has limits. For cortisol, the main ones are:

- This test measures total cortisol, nearly all of which is bound to a carrier protein. Conditions that raise or lower that protein — pregnancy, estrogen therapy, serious illness, liver disease, kidney disease — move the total up or down without changing the amount of active hormone.
- A single cortisol value rarely settles a diagnosis. Because the level swings with the time of day and with stress, both cortisol excess and cortisol deficiency are normally confirmed with stimulation or suppression protocols, or alongside other tests, rather than on one number.
- During metyrapone testing, a related steroid called 11-deoxycortisol builds up and is partly read as cortisol. That can make the result look higher than it is and hide an underactive adrenal gland.
- High bilirubin in the sample can raise the measured cortisol.
- A small number of patients carry natural antibodies in their blood — often people who work closely with animals or who have received certain antibody-based treatments — that can interfere with the test and produce an unexpected result.
- A cortisol result is one piece of a larger picture. It is meant to be read together with the patient's symptoms, medical history, and other test results — never on its own.

Reference Range(s):

Cortisol is measured in micrograms per deciliter ($\mu\text{g/dL}$). Because the level follows a daily rhythm, results are compared against the expected range for the time the sample was drawn:

- **Morning** (around 8 a.m., the daily peak): **5–25 $\mu\text{g/dL}$**
- **Afternoon and evening** (falling through the day): **about half the morning value**
- **Stimulation and suppression testing** results are judged against the patient's own starting value rather than a fixed range.

A result outside these ranges is not automatically a problem, and a result inside them does not rule one out. Only the ordering provider can interpret what a given number means for a given patient. Patients should always go by the reference range printed on their own laboratory report.

Analyte	Disorder	Expected Value*
Cortisol	PCOS / PMOS	N
Cortisol	Cushing syndrome	↑
Cortisol	Primary adrenal insufficiency	↓↓
Cortisol	Sheehan syndrome	↓
Cortisol	Acute infection or inflammation	↑

*N – Normal Range, ↓ – Decreased, ↓↓ – Markedly Decreased, ↑ – Increased.

What are some references that discuss the medical necessity of testing Cortisol?

1. Nieman LK, et al. The diagnosis of Cushing's syndrome: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, **93**, 1526–1540 (2008).
2. Bornstein SR, et al. Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, **101**, 364–389 (2016).
3. Fleseriu M, et al. Hormonal replacement in hypopituitarism in adults: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, **101**, 3888–3921 (2016).
4. Karaca Z, et al. Sheehan syndrome. *Nat Rev Dis Primers*, **2**, 16092 (2016).
5. Annane D, et al. Guidelines for the diagnosis and management of critical illness-related corticosteroid insufficiency in critically ill patients (part I). *Crit Care Med*, **45**, 2078–2088 (2017).
6. Teede HJ, et al. Recommendations from the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. *J Clin Endocrinol Metab*, **108**, 2447–2469 (2023).



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