

Adrenocorticotrophic Hormone (ACTH)

MDL Test Number: 661

Methodology: Immunoassay

CPT Codes: 82024



Specimen Collection Platform:

Plasma in EDTA (lavender-top) tube

Turnaround Time:

24 - 72 hours

Stability:

Refrigerate. Ship with a cold pack.

Test Additions*:

30 days to add tests



What is Adrenocorticotrophic Hormone (ACTH)?

Adrenocorticotrophic hormone (ACTH) is made by the pituitary, a small gland at the base of the brain. Its job is to signal the adrenal glands, which sit atop the kidneys, to produce cortisol. The hypothalamus signals the pituitary to release it, and the resulting cortisol feeds back to switch it off again, a self-correcting loop that keeps cortisol within a workable range from hour to hour (Figure 1).

Two features shape how the test is used. The level swings through the day, highest in the early morning and lowest in the evening, which is why the expected range is built around a draw at about nine in the morning. And ACTH is read together with a cortisol drawn at the same time rather than on its own. It is the pairing that shows whether a cortisol problem starts in the adrenal glands themselves or in the pituitary above them.

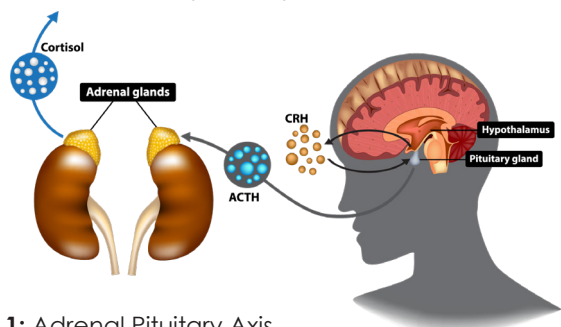


Figure 1: Adrenal Pituitary Axis

Specimen Collection:



1. Draw into a an EDTA tube, recording the time of collection.



2. Immediately after blood collection, invert the tube(s) gently 5 times to ensure mixing of anticoagulant.



3. Centrifuge for at least 15 minutes at 2200-2500 RPM.



4. Using a pipette, transfer the plasma to a transfer vial and ship with a frozen cold pack.

Why test for Adrenocorticotrophic Hormone (ACTH)?

ACTH is measured to locate the source of a cortisol problem rather than to detect one:

- **To separate adrenal from pituitary causes of low cortisol.** When the adrenal glands are the problem, ACTH climbs because the pituitary is pushing harder. When the pituitary is the problem, ACTH is low or normal at a time when it should be high.
- After a difficult delivery with heavy blood loss, **Sheehan syndrome** damages the pituitary at the time of birth and can present months or years later as fatigue, failure to breastfeed, or absent periods.
- **To find the source of too much cortisol.** In Cushing syndrome, ACTH is raised when the drive comes from a pituitary tumor or from a tumor elsewhere producing ACTH, and suppressed when the adrenal gland is making cortisol on its own.
- Where steroid treatment is suspected of suppressing the axis, which is by a wide margin the most common reason for a low ACTH. Recovery after treatment stops varies considerably between individuals, so the assessment is often repeated rather than settled on a single result.



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Special Instructions:

- **A morning draw:** ACTH is highest in the early morning and lowest in the evening, and the expected range assumes a sample taken at about nine in the morning. Draw at the time requested and record the exact time on the request; a later sample can look low when nothing is wrong.
- **This test needs its own tube:** ACTH is measured in chilled EDTA plasma — the liquid part of blood collected into a tube that prevents clotting — rather than in the standard tube used for most tests. The molecule is fragile: it degrades in a sample left at room temperature and sticks to ordinary glass, which is why the specimen is chilled, spun cold, and frozen without delay. It cannot be added to a sample already drawn, so it must be ordered before the draw.
- **Recent cosyntropin:** The manufacturer directs that ACTH not be measured after cosyntropin, the synthetic ACTH used in adrenal stimulation testing, because results may be falsely high or falsely low. Draw the ACTH before any stimulation test, not after.
- **Steroid medications:** Cortisol switches ACTH off, so steroid treatment in any form — tablets, inhalers, creams, or joint injections — lowers ACTH. Tell the ordering provider about every steroid being used, including ones that seem too small to matter.
- **Biotin supplements:** Biotin, sometimes sold as vitamin B7 and found in hair, skin, and nail products, can interfere with tests of this kind. This test showed no meaningful change up to 1500 nanograms per milliliter, well above what an ordinary supplement produces. Tell the ordering provider about any biotin being taken.

Limitations:

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

- The test reports results from 5 picograms per milliliter upward, and lower results are reported as less than 5. A low ACTH is itself a finding in pituitary causes of low cortisol and in Cushing syndrome, driven by the adrenal gland. Some of the results this test exists to find, therefore, sit at or below that point, and nothing about how the sample is taken changes it.
- An ACTH result means little without a cortisol drawn at the same time. The two are interpreted as a pair, and a value that looks normal on its own can be clearly wrong for the cortisol beside it.
- The test also picks up fragments of the ACTH molecule and a related pituitary peptide. These are not usually present in any quantity, but they are part of why an unexpected result is repeated rather than acted on immediately.
- Heterophilic antibodies — antibodies against animal proteins that some people carry — are more common in people routinely exposed to animals or animal products, and can produce an odd result. Asfotase alfa, a manufactured form of alkaline phosphatase used to treat hypophosphatasia, interferes with tests that detect using alkaline phosphatase. The manufacturer directs that samples from patients taking it be run by a different method.
- An ACTH 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):

Results are reported in picograms per milliliter (pg/mL). The expected range below comes from the manufacturer's study of 59 apparently healthy volunteers and assumes a morning draw, because the level falls throughout the day. Its lower end is not a number but an absence: a healthy person can carry too little ACTH in the blood for this method to measure it. In the morning, that is an ordinary finding rather than an abnormal one. Because the interval was established for a morning collection, a sample drawn later in the day is expected to be lower and cannot properly be compared against it.

- **Adults, morning draw: Not detectable to 46 pg/mL**
- **Median of that group: 24 pg/mL**

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*
ACTH	Primary adrenal insufficiency	↑↑
ACTH	Cushing syndrome	V
ACTH	Secondary adrenal insufficiency	↓
ACTH	Hypopituitarism (e.g. Sheehan)	↓

*V – Variable, ↓ – Decreased, ↑↑ – Markedly Increased.

What are some references that discuss the medical necessity of testing Adrenocorticotrophic Hormone (ACTH)?

1. Bornstein, S. R. et al. Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, **101**, 364–389 (2016).
2. Fleseriu, M. et al. Hormonal replacement in hypopituitarism in adults: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, **101**, 3888–3921 (2016).
3. Nieman, L. K. et al. The diagnosis of Cushing's syndrome: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, **93**, 1526–1540 (2008).
4. Karaca, Z. et al. Sheehan syndrome. *Nat Rev Dis Primers*, **2**, 16092 (2016).
5. Beuschlein, F. et al. European Society of Endocrinology and Endocrine Society joint clinical guideline: diagnosis and therapy of glucocorticoid-induced adrenal insufficiency. *J Clin Endocrinol Metab*, **109**, 1657–1683 (2024).



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