Test Definition: CRAV

Cortisol, Right Adrenal Vein, Serum

Overview

Useful For

Testing cortisol levels in the right adrenal vein

Second-order testing when cortisol measurement by immunoassay gives results that are not consistent with clinical symptoms, or if patients are known to, or suspected of, taking exogenous synthetic steroids

An adjunct in the differential diagnosis of primary and secondary adrenal insufficiency

An adjunct in the differential diagnosis of Cushing syndrome

Special Instructions

- Steroid Pathways

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

For confirming the presence of synthetic steroids, order SGSS / Synthetic Glucocorticoid Screen, Serum.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube: Red top
Specimen Volume: 1.5 mL Serum
Submission Container/Tube: Plastic vial
Collection Instructions:
1. Morning (8 a.m.) and afternoon (4 p.m.) specimens are preferred.
2. Include time of collection.
3. Centrifuge and aliquot serum into a plastic vial.

Additional Information: If multiple specimens are collected, send a separate order for each specimen.

Specimen Minimum Volume

Serum: 0.5 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Ambient	28 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Cortisol, the main glucocorticoid (representing 75%-95% of the plasma corticoids), plays a critical role in glucose metabolism and in the body's response to stress. Both hypercortisolism and hypocortisolism can cause disease.

Cortisol levels are regulated by corticotropin (previously adrenocorticotropic hormone, ACTH), which is synthesized by the pituitary in response to corticotropin releasing hormone (CRH). CRH is released in a cyclic fashion by the hypothalamus, resulting in diurnal peaks (6-8 a.m.) and troughs (11 p.m.) in plasma ACTH and cortisol levels.

The majority of cortisol circulates bound to corticosteroid-binding globulin and albumin. Normally, less than 5% of circulating cortisol is free (unbound). Free cortisol is the physiologically active form and is filterable by the renal glomerulus.

Pathological hypercortisolism due to endogenous or exogenous glucocorticoids is termed Cushing syndrome. Signs and symptoms of pathological hypercortisolism may include central obesity, hypertension, hyperglycemia, hirsutism, muscle weakness, and osteoporosis. However, these symptoms and signs are not specific for pathological hypercortisolism. The majority of individuals with some or all of the symptoms and signs will not suffer from Cushing syndrome.

When Cushing syndrome is present, the most common cause is iatrogenic, due to repeated or prolonged administration of, mostly, synthetic corticosteroids. Spontaneous Cushing syndrome is less common and results from either primary adrenal disease (adenoma, carcinoma, or nodular hyperplasia) or an excess of ACTH (from a pituitary tumor or an ectopic source). ACTH-dependent Cushing syndrome due to a pituitary corticotroph adenoma is the most frequently diagnosed subtype; most commonly seen in women in the third through fifth decades of life. The onset is insidious and usually occurs 2 to 5 years before a clinical diagnosis is made.

Hypocortisolism most commonly presents with nonspecific lassitude, weakness, hypotension, and weight loss. Depending on the cause, hyperpigmentation may be present. More advanced cases and patients submitted to physical

stress (ie, infection, spontaneous or surgical trauma) also may present with abdominal pain, hyponatremia, hyperkalemia, hypoglycemia, and in extreme cases, cardiovascular shock and renal failure.

The more common causes of hypocortisolism are:

Primary adrenal insufficiency:
-Addison disease
-Congenital adrenal hyperplasia, defects in enzymes involved in cortisol synthesis

Secondary adrenal insufficiency:
-Prior, prolonged corticosteroid therapy
-Pituitary insufficiency
-Hypothalamic insufficiency

For more information see Steroid Pathways.

Reference Values

No established reference values

Interpretation

In primary adrenal insufficiency, corticotropin (previously adrenocorticotropic hormone, ACTH) levels are increased and cortisol levels are decreased; in secondary adrenal insufficiency both ACTH and cortisol levels are decreased.

When symptoms of glucocorticoid deficiency are present and the 8 a.m. plasma cortisol value is less than 10 mcg/dL (or the 24-hour urinary free cortisol value is <50 mcg/24 hours), further studies are needed to establish the diagnosis. The 3 most frequently used tests are the ACTH (cosyntropin) stimulation test, the metyrapone test, and insulin-induced hypoglycemia test. First, the basal plasma ACTH concentration should be measured, and the short cosyntropin stimulation test performed.

Cushing syndrome is characterized by increased serum cortisol levels. However, the 24-hour urinary free cortisol excretion is the preferred screening test for Cushing syndrome, specifically CORTU / Cortisol, Free, 24 Hour, Urine that utilizes liquid chromatography-tandem mass spectrometry. A normal result makes the diagnosis unlikely.

Symptoms or signs of Cushing syndrome in a patient with low serum and urine cortisol levels suggest possible exogenous synthetic steroid effects.

Cautions

When cortisol assays are used for serial monitoring, the same methodology should be used throughout.

There is little, if any, value in an isolated p.m. serum cortisol measurement.

The most common cause of increased plasma cortisol levels in women is a high circulating concentration of estrogen (ie, estrogen therapy, pregnancy) resulting in increased concentration of corticosteroid-binding globulin. This does not result in an increase in the free, bioactive cortisol fraction. For this reason, measurement of 24-hour urinary free cortisol (CORTU / Cortisol, Free, 24 Hour, Urine) or demonstration of absent diurnal variation (ie, by midnight salivary cortisol measurement SALCC / Cortisol and Cortisone, Saliva) are the preferred means of diagnosing spontaneous Cushing

syndrome.

Acute stress (including hospitalization and surgery), alcoholism, depression, and many drugs (ie, exogenous cortisones, anticonvulsants) can obliterate normal diurnal variation, affect response to suppression/stimulation tests, and cause elevated baseline levels.

A low plasma cortisol level does not give conclusive indication of congenital adrenal hyperplasia. DCORT / 11-Deoxycortisol, Serum; OHPG / 17-Hydroxyprogesterone, Serum; and DHEA_ / Dehydroepiandrosterone (DHEA), Serum provide a more accurate and specific determination of the enzyme deficiency.

Clinical Reference

1. Lin CL, Wu TJ, Machacek DA, Jiang NS, Kao PC. Urinary free cortisol and cortisone determined by high-performance liquid chromatography in the diagnosis of Cushing's syndrome. J Clin Endocrinol Metab. 1997;82(1):151-155. doi:10.1210/jcem.82.1.3687
2. Findling JW, Raff H. Diagnosis and differential diagnosis of Cushing's syndrome. Endocrinol Metab Clin North Am. 2001;30(3):729-747. doi:10.1016/s0889-8529(05)70209-7
3. Buchman Al. Side effects of corticosteroid therapy. J Clin Gastroenterol. 2001;33(4):289-297. doi:10.1097/00004836-200110000-00006
4. Dodds HM, Taylor PJ, Cannell GR, Pond SM. A high-performance liquid chromatography-electrospray-tandem mass spectrometry analysis of cortisol and metabolites in placental perfusate. Anal Biochem. 1997;247(2):342-347. doi:10.1006/abio.1997.2074
5. Anna Nordenstrom and Henrik Falhammar. Diagnosis and management of the patient with non-classic CAH due to 21-hydroxylase deficiency European Journal of Endocrinology (2019) 180(3), R127-R145
6. Cengiz H, Demirci T, Varim C, Cetin S. Establishing a new screening 17 hydroxyprogesterone cut-off value and evaluation of the reliability of the long intramuscular ACTH stimulation test in the diagnosis of nonclassical congenital adrenal hyperplasia. Eur Rev Med Pharmacol Sci. 2021;25(16):5235-5240. doi:10.26355/eurrev_202108_26537

Performance

Method Description

Deuterated cortisol (d4-cortisol) is added to each specimen as an internal standard. Cortisol and d4-cortisol are extracted from the samples with methylene chloride and analyzed by liquid chromatography tandem mass spectrometry using multiple reaction monitoring. A calibration curve is included with each batch of patient samples.(Taylor RL, Machacek D, Singh RJ. Validation of a high-throughput liquid chromatographytandem mass spectrometry method for urinary cortisol and cortisone. Clin Chem. 2002;48[9]1511-1519)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

2 to 5 days

Test Definition: CRAV

Cortisol, Right Adrenal Vein, Serum

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

82533

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CRAV	Cortisol, RAV	2143-6

Result ID	Test Result Name	Result LOINC® Value
6345	Cortisol, RAV	2143-6