MAYO CLINIC LABORATORIES

Test Definition: COCOU

Cortisol/Cortisone, Free, 24 Hour, Urine

Overview

Useful For

Screening test for Cushing syndrome (hypercortisolism)

Assisting in diagnosing acquired or inherited abnormalities of 11-beta-hydroxysteroid dehydrogenase (cortisol to cortisone ratio)

Diagnosis of pseudo-hyperaldosteronism due to excessive licorice consumption

This test has limited usefulness in the evaluation of adrenal insufficiency.

Special Instructions

- Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Urine

Necessary Information

24-Hour volume (in milliliters) is required.

Specimen Required

Supplies: Urine Tubes, 10-mL (T068)
Submission Container/Tube: Plastic, urine tube (T068)
Specimen Volume: 5 mL
Collection Instructions:
1. Add 10 g of boric acid as preservative at the start of the collection.
2. Collect urine for a full 24 hours (required) and record the total volume.
Additional Information: See Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens for multiple collections.

Urine Preservative Collection Options

Note: The addition of preservative or application of temperature controls **must occur at the start** of the collection.

Ambient (no additive)	No
Refrigerate (no additive)	OK
Frozen (no additive)	OK
50% Acetic Acid	OK
Boric Acid	Preferred
Diazolidinyl Urea	No
6M Hydrochloric Acid	No
6M Nitric Acid	No
Sodium Carbonate	No
Toluene	No

Specimen Minimum Volume

3 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Refrigerated (preferred)	14 days	
	Ambient	72 hours	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Cortisol is a steroid hormone synthesized from cholesterol through a multienzyme pathway in the adrenal glands. It is the primary glucocorticoid in humans and acts as a gene transcription factor influencing a multitude of cellular responses in nearly all tissues. Cortisol plays a critical role in glucose metabolism, maintenance of vascular tone, immune response regulation, and in the physiologic response to stress. Its production is regulated by hypothalamic-pituitary feedback.

Only a small percentage of circulating cortisol is biologically active (free), with the majority of cortisol inactive because it is protein bound. As plasma cortisol concentrations increase, free cortisol (ie, unconjugated cortisol or hydrocortisone) also increases and is filtered by the glomeruli. Urinary free cortisol (UFC) correlates well with plasma free cortisol concentrations and reflects excretion of the circulating, biologically active, free cortisol associated with the signs and symptoms of hypercortisolism.

Urinary free cortisol testing is sensitive for the various types of adrenocortical dysfunction, particularly hypercortisolism (Cushing syndrome). Measurement of 24-hour UFC excretion by liquid chromatography tandem mass spectrometry (LC-MS/MS) is the preferred screening test for Cushing syndrome. LC-MS/MS methodology eliminates analytical

interference from substances such as carbamazepine (Tegretol) and synthetic corticosteroids, which can affect immunoassay-based cortisol results.

Cortisone, a downstream metabolite of cortisol, provides an additional information for diagnosing adrenal disorders, including abnormalities of 11-beta-hydroxysteroid dehydrogenase (11-beta HSD), the enzyme that converts cortisol to cortisone. Deficiency of 11-beta HSD can cause mineralocorticoid excess because cortisol, unlike cortisone, acts as a mineralocorticoid receptor agonist. Licorice (active component glycyrrhetinic acid) inhibits 11-beta HSD and excess consumption can produce similar effects.

Reference Values

CORTISOL
0-2 years: not established
3-8 years: 1.4-20 mcg/24 h
9-12 years: 2.6-37 mcg/24 h
13-17 years: 4.0-56 mcg/24 h
> or =18 years: 3.5-45 mcg/24 h

CORTISONE
0-2 years: not established
3-8 years: 5.5-41 mcg/24 h
9-12 years: 9.9-73 mcg/24 h
13-17 years: 15-108 mcg/24 h
> or =18 years: 17-129 mcg/24 h

For International System of Units (SI) conversion for Reference Values, see
www.mayocliniclabs.com/order-tests/si-unit-conversion.html

Interpretation

Most patients with Cushing syndrome have increased 24-hour urinary excretion of cortisol and/or cortisone. Further studies, including suppression or stimulation tests, measurement of serum corticotropin (adrenocorticotropic hormone) concentrations, and imaging are usually necessary to confirm the diagnosis and determine the etiology.

Values in the normal range may occur in patients with mild Cushing syndrome or with periodic hormonogenesis. In these cases, continuing follow-up and repeat testing are necessary to confirm the diagnosis.

Patients with Cushing syndrome due to intake of synthetic glucocorticoids should have both suppressed cortisol and cortisone. In these circumstances, a synthetic glucocorticoid screen may be ordered (SGSU / Synthetic Glucocorticoid Screen, Random, Urine).

Suppressed cortisol and cortisone values may also be observed in primary adrenal insufficiency and hypopituitarism. However, random urine specimens are not useful for evaluation of hypocorticalism. However, many normal individuals may exhibit a very low 24-hour urinary cortisol excretion with considerable overlap with the values observed in pathological hypocorticalism. Therefore, without other tests, 24-hour urinary cortisol measurements cannot be relied upon for the diagnosis of hypocorticalism.

Patients with 11-beta hydroxysteroid dehydrogenase deficiency may have cortisone to cortisol ratios less than 1,

whereas a ratio of 2:1 to 3:1 is seen in normal patients. Excessive licorice consumption and use of carbenoxolone, a synthetic derivative of glycyrrhizinic acid used to treat gastroesophageal reflux disease, also may suppress the ratio to less than 1.

Cautions

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

Liquid chromatography tandem mass spectrometry eliminates analytical interferences including carbamazepine (Tegretol) and synthetic corticosteroids.

This test has limited usefulness in the evaluation of adrenal insufficiency.

Improper collection may alter results. For example, a missed morning collection may result in false-negative tests; an extra morning collection (ie, >24 hours) may give false-positive results.

Kidney disease (decreased clearance) may cause falsely-low values.

Values may be elevated to twice normal in pregnancy.

Patients with exogenous Cushing syndrome caused by ingestion of hydrocortisone will not have suppressed cortisol and cortisone values.

Clinical Reference

1. 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
2. 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 Endo Metab 1997;82(1):151-155 3. Eisenhofer G, Grebe S, Cheung NK V. Monoamine-producing tumors. In: Rifai N, Horvath AR, Wittwer CT, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:1421

Performance

Method Description

Cortisol and cortisone are extracted from supernatant by an online extraction utilizing high throughput liquid chromatography. This is followed by conventional liquid chromatography and analysis on a tandem mass spectrometer equipped with a heated nebulizer ion source. Deuterated cortisol (d4-cortisol, d7-cortisone) is added to a 0.1 mL sample as an internal standard. Cortisol, cortisone, and d4-cortisol are extracted from the specimens using online turbulent flow high-performance liquid chromatography extraction.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed
Monday through Friday

Report Available
2 to 7 days

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
82530-Cortisol; free
82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
COCOU	Cortisol/Cortisone, Free, U	101319-2

Result ID	Test Result Name	Result LOINC® Value
8546	Cortisol, U	14158-0
10327	Cortisone, U	14044-2
TM93	Collection Duration (h)	13362-9
VL47	Volume (mL)	3167-4