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-hydroxy steroid 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. Collect urine for 24 hours.
2. Add 10 g of boric acid as preservative at start of collection.
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
Refrigerate	OK
Frozen	OK
50% Acetic Acid	OK
Boric Acid	Preferred
Diazolidinyl Urea	No
6M Hydrochloric Acid	No
6M Nitric Acid	No
Sodium Carbonate	No
Thymol	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	
	Frozen	28 days	
	Ambient	72 hours	

Clinical & Interpretive

Clinical Information

Cortisol is a steroid hormone synthesized from cholesterol by a multienzyme cascade in the adrenal glands. It is the main glucocorticoid in humans and acts as a gene transcription factor influencing a multitude of cellular responses in virtually all tissues. Cortisol plays a critical role in glucose metabolism, maintenance of vascular tone, immune response regulation, and in the body's response to stress. Its production is under hypothalamic-pituitary feedback control.

Only a small percentage of circulating cortisol is biologically active (free), with the majority of cortisol inactive (protein bound). As plasma cortisol values increase, free cortisol (ie, unconjugated cortisol or hydrocortisone) increases and is filtered through the glomerulus. Urinary free cortisol (UFC) correlates well with the concentration of plasma free cortisol. UFC represents excretion of the circulating, biologically active, free cortisol that is responsible for the signs and symptoms of hypercortisolism. UFC is a sensitive test for the various types of adrenocortical dysfunction, particularly hypercortisolism (Cushing syndrome). A 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 interferences including carbamazepine (Tegretol) and synthetic corticosteroids, which can affect immunoassay-based cortisol results.

Cortisone, a downstream metabolite of cortisol, provides an additional variable to assist in the diagnosis of various adrenal disorders, including abnormalities of 11-beta-hydroxy steroid dehydrogenase (11-beta HSD), the enzyme that converts cortisol to cortisone. Deficiency of 11-beta HSD results in a state of mineralocorticoid excess because cortisol (but not cortisone) acts as a mineralocorticoid receptor agonist. Licorice (active component glycyrrhetinic acid) inhibits 11-beta HSD and excess consumption can result in similar changes.

Reference Values

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

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

Use the factors below to convert each analyte from mcg/24 hours to nmol/24 hours:

Conversion factors
Cortisol: mcg/24 hours x 2.76=nmol/24 hours (molecular weight=362.5)
Cortisone: mcg/24 hours x 2.78=nmol/24 hours (molecular weight=360)

For SI unit Reference Values, see https://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 might be ordered (call 800-533-1710).

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. Further, many normal individuals also 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 HSD deficiency may have cortisone to cortisol ratios <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 <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.

This methodology (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.

Renal 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. Findling JW, Raff H: Diagnosis and differential diagnosis of Cushing's syndrome. Endocrinol Metab Clin North Am 2001;30:729-747
2. Boscaro M, Barzon L, Fallo F, Sonino N: Cushing's syndrome. Lancet 2001;357:783-791
3. Taylor RL, Machacek D, Singh RJ: Validation of a high-throughput liquid chromatography-tandem mass spectrometry method for urinary cortisol and cortisone. Clin Chem 2002;48:1511-1519

Performance

Method Description

Deuterated cortisol (d3-cortisol) is added to a 0.1-mL urine specimen as an internal standard. Cortisol, cortisone, and d3-cortisol are extracted from the specimens using online turbulent-flow HPLC and analyzed by liquid chromatography-tandem mass spectrometry using multiple-reaction monitoring in positive mode. The following ion pairs are used for analysis: Cortisol (363.0/121.1); Cortisone (361.0/163.0); d3-Cortisol (366.0/121.2). A calibration curve, generated from stripped urine spiked standards, is included with each batch of patient specimens.(Taylor RL, Machacek DA, Singh RJ: Validation of a high-throughput liquid chromatography-tandem mass spectrometry method for urinary cortisol and cortisone. Clin Chem 2002;48:1511-1519)

PDF Report

No

Day(s) Performed
Monday through Saturday

Report Available
2 to 5 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

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	13362-9
VL47	Urine Volume	3167-4