MAYO CLINIC LABORATORIES

Test Definition: CORTU

Cortisol, Free, 24 Hour, Urine

Overview

Useful For

Preferred screening test for Cushing syndrome

Diagnosis of pseudo-hyperaldosteronism due to excessive licorice consumption

Test **may not be useful** 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
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 **must occur prior to the start of** the collection or application of temperature controls **must occur during 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	7 days	

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) in the urine 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.

Reference Values

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

Use the factor below to convert from mcg/24 hours to nmol/24 hours:

Conversion factor
Cortisol: mcg/24 hours x 2.76=nmol/24 hours (molecular weight=362.5)

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. Further studies, including suppression or stimulation tests, measurement of serum corticotrophin 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 suppressed cortisol. In these circumstances a synthetic glucocorticoid screen might be ordered (SGSU / Synthetic Glucocorticoid Screen, Urine).

Suppressed cortisol values may also be observed in primary adrenal insufficiency and hypopituitarism. However, many normal individuals may also 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.

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 test has limited usefulness in the evaluation of adrenal insufficiency.

This methodology (liquid chromatography-tandem mass spectrometry) eliminates analytical interferences including carbamazepine (Tegretol) and synthetic corticosteroids.

Renal disease (decreased excretion) may cause falsely low 24-hour urinary free cortisol values.

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.

Twenty-four hour urinary free cortisol values may be elevated to twice the upper limit of the normal range during

pregnancy.

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

Supportive Data

In Mayo's reference value study, gender was found to significantly influence cortisol values (*P* value=0.001). However, while this was statistically significant, gender explained only 6% of the variability in cortisol normal ranges and, therefore, was not considered to have a clinically significant impact on cortisol reference 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
4. Eisenhofer G, Grebe S, Cheung N-K V: Chapter 63 Monoamine-Producing Tumors. In Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. Sixth edition. Edited by N Rafai, AR Horvath, CT Wittwer. Elsevier, 2018. pp 1421
5. Luo A, El Gierari ETM, Nally LM, et al: Clinical utility of an ultrasensitive urinary free cortisol assay by tandem mass spectrometry. Steroids. 2019 Jun;146:65-69. doi: 10.1016/j.steroids.2019.03.014

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 Friday

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

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CORTU	Cortisol, Free, U	43126-2

Result ID	Test Result Name	Result LOINC® Value
8546	Cortisol, U	14158-0
TM93	Collection Duration	13362-9
VL47	Urine Volume	3167-4