MAYO CLINIC LABORATORIES

Test Definition: CRANR

Cortisol, Free, Random, U

Overview

Useful For

Investigating suspected hypercortisolism when a 24-hour collection is prohibitive (ie, pediatric patients)

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
CRAN	Cortisol, Random, U	No	Yes
CRETR	Creatinine, Random, U	Yes	Yes

Method Name

CRAN: Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)
CRETR: Enzymatic Colorimetric Assay

NY State Available

Yes

Specimen

Specimen Type

Urine

Ordering Guidance

The preferred screening test for Cushing syndrome is a measurement of free cortisol in a 24-hour urine collection by liquid chromatography-tandem mass spectrometry (LC-MS/MS); order CORTU / Cortisol, Free, 24 Hour, Urine.
The optimal specimen type for evaluation of primary adrenal insufficiency and hypopituitarism is serum; order CORT / Cortisol, Serum.

Specimen Required

Supplies: Urine tube, 10 mL (T068)
Collection Container/Tube: Clean, plastic urine container with no metal cap or glued insert
Submission Container/Tube: Plastic, 10-mL urine tube or clean, plastic aliquot container with no metal cap or glued insert
Specimen Volume: 10 mL
Collection Instructions: Collect a random urine specimen.

Reject Due To

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

Specimen Minimum Volume

4 mL

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) 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

Males

0-2 years: 3.0-120 mcg/g creatinine

3-8 years: 2.2-89 mcg/g creatinine

9-12 years: 1.4-56 mcg/g creatinine

13-17 years: 1.0-42 mcg/g creatinine

> or =18 years: 1.0-119 mcg/g creatinine

Females

0-2 years: 3.0-120 mcg/g creatinine

3-8 years: 2.2-89 mcg/g creatinine

9-12 years: 1.4-56 mcg/g creatinine

13-17 years: 1.0-42 mcg/g creatinine

> or =18 years: 0.7-85 mcg/g creatinine

Use the conversion factors below to convert each analyte from mcg/g creatinine to nmol/mol creatinine.

Conversion factor

Cortisol: mcg/g creatinine x 312=nmol/mol creatinine

Cortisol molecular weight=362.5

Creatinine molecular weight=113.12

Interpretation

Most patients with Cushing syndrome have increased 24-hour urinary excretion of cortisol. 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 suppressed cortisol. In these circumstances a synthetic glucocorticoid screen might be ordered (SGSU / Synthetic Glucocorticoid Screen, Random, Urine).
Suppressed cortisol values may also be observed in primary adrenal insufficiency and hypopituitarism. The optimal specimen type for evaluation of primary adrenal insufficiency and hypopituitarism is serum (CORT / Cortisol, Serum).

Cautions

Random urine cortisol results are less reliable than results obtained from properly collected and complete 24-hour urine specimens, which are not affected by diurnal variations in cortisol levels.
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 methodology eliminates analytical interferences including carbamazepine (Tegretol) and synthetic corticosteroids.
Random urine specimens may yield falsely elevated values when patients have a high urinary output.
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 values.
When N-acetylcysteine is administered at levels sufficient to act as an antidote for the treatment of acetaminophen overdose, it may lead to falsely decreased creatinine results.

Supportive Data

Multiple calibration curves for urinary cortisol and cortisone exhibited consistent linearity and reproducibility in the range of 7 to 828 nmol/L (0.25-30 mcg/dL). Inter-assay coefficients of variation were 7.3% to 16% for mean concentrations of 6 to 726 nmol/L (0.2-26.3 mcg/dL) for cortisol and cortisone. The detection limit was 6 nmol/L (0.2 mcg/dL). Recovery of cortisol and cortisone added to urine was 97% to 123%. The regression equation for the liquid chromatography-tandem mass spectrometry (LC-MS/MS) (y) and high performance liquid chromatography (x) method for cortisol was: y = 1.11x + 0.03 mcg cortisol/24 h (r(2) = 0.992; n = 99). The regression equation for the LC-MS/MS (y) and immunoassay (x) methods for cortisol was: y = 0.66x - 12.1 mcg cortisol/24 h (r(2) = 0.67; n = 99).(1)

Clinical Reference

1. 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
2. Findling JW, Raff H: Diagnosis and differential diagnosis of Cushing's syndrome. Endocrinol Metab Clin North Am. 2001;30:729-747
3. Boscaro M, Barzon L, Fallo F, Sonino N: Cushing's syndrome. Lancet 2001;357:783-791
4. Suzuki S, Minamidate T, Shiga A, et al. Steroid metabolites for diagnosing and predicting clinicopathological features in cortisol-producing adrenocortical carcinoma.BMC Endocr Disord. 2020;20(1):173. doi: 10.1186/s12902-020-00652-y

Performance

Method Description

Cortisol:

Deuterated cortisol (d[3]-cortisol) is added to a 0.1-mL urine specimen as an internal standard. Cortisol, cortisone, and d(3)-cortisol are extracted from the specimens using online turbulent-flow high-performance liquid chromatography 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), d(3)-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;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)

Creatinine:

The enzymatic method is based on the determination of sarcosine from creatinine with the aid of creatininase, creatinase, and sarcosine oxidase. The liberated hydrogen peroxide is measured via a modified Trinder reaction using a colorimetric indicator. Optimization of the buffer system and the colorimetric indicator enables the creatinine concentration to be quantified both precisely and specifically.(Package insert: Creatinine plus ver 2. Roche Diagnostics; V15.0, 03/2019)

PDF Report

No

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

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

CPT Code Information

82530

82570