

## 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, (order RCTUR )	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.

### 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	7 days	
	Frozen	28 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.

The UFC assay 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

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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 (adrenocorticotrophic 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.

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 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 ( $r^2 = 0.67$ ;  $n = 99$ ).<sup>(1)</sup>

**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(9):1511-1519
2. Findling JW, Raff H. Diagnosis and differential diagnosis of Cushing's syndrome. *Endocrinol Metab Clin North Am*. 2001;30(3):729-747
3. Boscaro M, Barzon L, Fallo F, Sonino N. Cushing's syndrome. *Lancet*. 2001;357(9258):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**

Isotopically labeled cortisol and cortisone are added to the sample as internal standards. Cortisol, cortisone, and coinciding internal standards are extracted from the specimens using online turbulent flow chromatography, which is followed by liquid chromatography tandem mass spectrometry analysis.(Unpublished Mayo method)

**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

**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

82570

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
CRANR	Cortisol, Free, Random, U	44309-3

Result ID	Test Result Name	Result LOINC® Value
10328	Cortisol/Creatinine Ratio	11155-9
CRETR	Creatinine, Random, U	2161-8