Test Definition: CCFR

Cortisol/Cortisone, Free, Random, Urine

Overview

Useful For

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

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

Diagnosis of pseudohyperaldosteronism due to excessive licorice consumption

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

This test is **not useful for** evaluation of hypocorticalism.

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
COCOR	Cortisol, Random, U	No	Yes
CRETR	Creatinine, Random, U	Yes, (order RCTUR)	Yes

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Urine

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

5 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 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. It 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
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

CORTISONE
0-2 years: 25-477 mcg/g creatinine
3-8 years: 11-211 mcg/g creatinine
9-12 years: 5.8-109 mcg/g creatinine
13-17 years: 5.4-102 mcg/g creatinine
18-29 years: 5.7-153 mcg/g creatinine
30-39 years: 6.6-176 mcg/g creatinine
40-49 years: 7.6-203 mcg/g creatinine
50-59 years: 8.8-234 mcg/g creatinine
60-69 years: 10-270 mcg/g creatinine
> or =70 years: 12-311 mcg/g creatinine

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

Conversion factors
Cortisol: mcg/g creatinine x 312=nmol/mol creatinine
Cortisone: mcg/g creatinine x 314=nmol/mol creatinine

Cortisol molecular weight=362.5
Cortisone molecular weight=360.4
Creatinine molecular weight=113.12

CREATININE
<18 years: Not established
> or =18 years: 16-326 mg/dL

Interpretation

Most patients with Cushing syndrome have increased urinary excretion of cortisol and/or cortisone. 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 both suppressed cortisol and cortisone. In these circumstances a synthetic glucocorticoid screen might 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.

Patients with 11-beta-hydroxy steroid dehydrogenase deficiency may have cortisone to cortisol ratios less than 1, whereas a ratio of 2 or 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

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 alter 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 and cortisone 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.

Clinical Reference

1. 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(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
5. Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. Lancet Diabetes Endocrinol. 2021;9(12):847-875. doi:10.1016/S2213-8587(21)00235-7

Performance

Method Description

Cortisol and Cortisone:
Isotopically labeled cortisol and cortisone internal standards are added to 0.1 mL of urine sample. The cortisol, cortisone, and internal standards are then extracted from the specimens using online turbulent flow high-performance liquid chromatography extraction. This is followed by conventional liquid chromatography and measured using a tandem mass spectrometer.(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

82542
82530 - Cortisol
82570 - Creatinine

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CCFR	Cortisol/Cortisone, Free, Random, U	In Process

Result ID	Test Result Name	Result LOINC® Value
10328	Cortisol/Creatinine Ratio	11155-9
10329	Cortisone/Creatinine Ratio	30511-0
CRETR	Creatinine, Random, U	2161-8