

Free Cortisol and Cortisone in Urine

USED TO MEASURE THE CONCENTRATIONS OF UNCONJUGATED CORTISOL AND CORTISONE IN URINE

Clinical Background

Abnormal changes in cortisol levels may be due to hypothalamic, pituitary, or adrenal dysfunction. If undiagnosed and untreated, these disorders can be life threatening. In the diurnal rhythm of normal individuals, peak levels of cortisol are seen in the serum in the morning (6:00 a.m.), and the lowest levels are in the late evening (10:00 p.m.). These normal individuals will show cortisol suppression in response to dexamethasone administration. The dexamethasone-suppression test is usually utilized for the evaluation and the differential diagnosis of patients with Cushing syndrome. Urinary-free cortisol is an excellent test for the diagnosis of endogenous Cushing syndrome and for assessing responses to dexamethasone-suppression tests. One of the pathways of cortisol inactivation is through a conversion to cortisone. A combined test for urinary-free cortisol and cortisone can be useful in evaluating patients with apparent mineralocorticoid excess (AME) syndrome, congenital adrenal hyperplasia, and adrenal insufficiency.

Indications for Ordering

- Cortisol levels may be elevated due to adrenal adenoma or carcinoma, increased adrenal response to excess ACTH production, from a pituitary adenoma, or “ectopic ACTH” production by a tumor of nonendocrine tissue or exogenous administration of cortisol, which is present in some anti-inflammatory drugs. Hypocortisolism may be produced by adrenal disease or atrophy (Addison disease) or secondarily by the loss of ACTH production by the pituitary.
- The AME syndrome is an inherited form of hypertension resulting from insufficiency of the enzyme 11- β -hydroxysteroid dehydrogenase type 2 (11- β -HSD2), which is required for conversion of cortisol to cortisone. The diagnosis of AME can be based on the ratio of urinary-free cortisol and cortisone. Normal values for the ratio of urinary-free cortisol concentrations to urinary-free cortisone are usually less than 0.5, while a higher ratio is observed in patients with hypertension attributable to AME syndrome. In addition to AME syndrome, the 11- β -HSD2 enzyme can be inhibited by licorice, carbenoxolone, and some other drugs that would lead to an increased ratio of cortisol to cortisone. Another enzyme, 11- β -HSD1, is responsible for the conversion of cortisone to cortisol. Decreased 11- β -HSD1 activity can be a reason for reduced efficacy of cortisone treatment.

Interpretation

- Urinary-free cortisol concentrations increase with Cushing disease, an adrenal adenoma and carcinoma, a pituitary adenoma, some other cancers (especially lung), the use of anti-inflammatory drugs containing cortisol or cortisone, and with depression and stress.
- Urinary-free cortisol concentrations decrease with Addison disease, exogenous Cushing syndrome, pituitary insufficiency, and deficient hypothalamic secretion of corticotropin-releasing hormone.
- If the ratio of cortisol to cortisone is above 0.5 and the cortisol concentration is within the reference interval, then this is an indication of an apparent mineralocorticoid excess syndrome and low activity of the 11- β -HSD2 enzyme.
- If the ratio of cortisol to cortisone is below 0.15 and the cortisol concentration is within the reference interval, then this is an indication of low activity of the 11- β -HSD1 enzyme.

Methodology

The measurement of unconjugated cortisol and cortisone in the urine is accomplished by a chromatographic separation using HPLC, followed by tandem mass spectrometry to separate and specifically measure the compounds with characteristic parent and daughter mass ions of cortisol and cortisone. The inherent high specificity of tandem mass spectrometry is enhanced by the measurement of two product ions for each compound. This measurement results in a very specific analysis utilizing qualitative confirmation of the compound's identity in every sample and the elimination of nearly all potentially interfering substances.

References

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5. Meikle AW, West CD. Laboratory tests for the diagnosis of Cushing's syndrome and adrenal insufficiency and factors affecting those tests. In *Endocrinology*, vol 2. DeGroot L, et al, eds. 1986; New York: Grune & Stratton, Inc., 1157-78.

Test Information

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Cortisol/Cortisone Urine Free by LC-MS/MS

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.