Overview

Useful For
Diagnostic workup of patients with congenital adrenal hyperplasia

Part of metyrapone testing in the workup of suspected secondary or tertiary adrenal insufficiency

Part of metyrapone testing in the differential diagnostic workup of Cushing syndrome

Testing Algorithm
See Steroid Pathways in Special Instructions.

Special Instructions
- Steroid Pathways

Method Name
Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Serum

Necessary Information
Indicate if specimen was drawn before or after metyrapone.

Specimen Required
Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 0.5 mL

Collection Instructions: Morning (8 a.m.) specimen is preferred.

Specimen Minimum Volume
0.4 mL

Reject Due To

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>OK</td>
</tr>
<tr>
<td>Gross icterus</td>
<td>OK</td>
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</tbody>
</table>
Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ambient</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>28 days</td>
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Clinical and Interpretive

Clinical Information

11-Deoxycortisol (Compound S) is the immediate precursor of cortisol:

\[
\text{11 \beta-hydroxylase} \quad \text{11-deoxycortisol} \rightarrow \text{cortisol}
\]

Compound S is typically increased when adrenocorticotropic hormone (ACTH) levels are increased (eg, Cushing disease, ACTH-producing tumors) or in 11 beta-hydroxylase deficiency, a rare subform of congenital adrenal hyperplasia (CAH). In CAH due to 11 beta-hydroxylase deficiency, cortisol levels are low, resulting in increased pituitary ACTH production and increased serum and urine 11-deoxycortisol levels.

Pharmacological blockade of 11 beta-hydroxylase with metyrapone can be used to assess the function of the hypothalamic-pituitary-adrenal axis (HPA). In this procedure metyrapone is administered to patients, and serum 11-deoxycortisol levels or urinary 17-hydroxy steroid levels are measured either at baseline (midnight) and 8 hours later (overnight test), or at baseline and once per day during a 2-day metyrapone test (4-times a day metyrapone administration over 2 days). Two-day metyrapone testing has been largely abandoned because of the logistical problems of multiple timed urine and blood collections and the fact that overnight testing provides very similar results. In either case, the normal response to metyrapone administration is a fall in serum cortisol levels, triggering a rise in pituitary ACTH secretion, which, in turn, leads to a rise in 11-deoxycortisol levels due to the ongoing 11-deoxycortisol-to-cortisol conversion block.

In the diagnostic workup of suspected adrenal insufficiency, the results of overnight metyrapone testing correlate closely with the gold standard of HPA-axis assessment, insulin hypoglycemia testing. Combining 11-deoxycortisol measurements with ACTH measurements during metyrapone testing further enhances the performance of the test. Impairment of any component of the HPA-axis results in a subnormal rise in 11-deoxycortisol levels. By contrast, standard-dose or low-dose ACTH(1-24) (cosyntropin)-stimulation testing, which forms the backbone for diagnosis of primary adrenal failure (Addison disease), only assess the ability of the adrenal cells to respond to ACTH stimulation. While this allows unequivocal diagnosis of primary adrenal failure, in the setting of secondary or tertiary adrenal insufficiency, metyrapone testing is more sensitive and specific than either standard-dose or low-dose ACTH(1-24)-stimulation testing.

Metyrapone testing is also sometimes employed in the differential diagnosis of Cushing syndrome. In Cushing disease (pituitary-dependent ACTH overproduction), the ACTH-hypersecreting pituitary tissue remains responsive to the usual feedback stimuli, just at a higher "set-point" than in the normal state, resulting in increased ACTH secretion and 11-deoxycortisol production after metyrapone administration. By contrast, in Cushing syndrome due to primary...
adrenal corticosteroid oversecretion or ectopic ACTH secretion, pituitary ACTH production is appropriately shut down and there is usually no further rise in ACTH and, hence 11-deoxycortisol, after metyrapone administration. The metyrapone test has similar sensitivity and specificity to the high-dose dexamethasone suppression test in the differential diagnosis of Cushing disease, but is less widely used because of the lack of availability of an easy, automated 11-deoxycortisol assay. In recent years, both tests have been supplanted to some degree by corticotropin-releasing hormone (CRH)-stimulation testing with petrosal sinus serum ACTH sampling.

See Steroid Pathways in Special Instructions.

Reference Values

< or =18 years: <344 ng/dL

>18 years: 10-79 ng/dL

For SI unit Reference Values, see https://www.mayocliniclabs.com/order-tests/si-unit-conversion.html

Interpretation

In a patient suspected of having congenital adrenal hyperplasia (CAH), elevated serum 11-deoxycortisol levels indicate possible 11 beta-hydroxylase deficiency. However, not all patients will show baseline elevations in serum 11-deoxycortisol levels. In a significant proportion of cases, increases in 11-deoxycortisol levels are only apparent after adrenocorticotropic hormone (ACTH)(1-24) stimulation.(1)

Serum 11-deoxycortisol levels below 1,700 ng/dL 8 hours after metyrapone administration is indicative of probable adrenal insufficiency. The test cannot reliably distinguish between primary and secondary or tertiary causes of adrenal failure, as neither patients with pituitary failure, nor those with primary adrenocortical failure, tend to show an increase of 11-deoxycortisol levels after metyrapone is administered.

See Steroid Pathways in Special Instructions.

Cautions

Ethanol, estrogens (exogenous and pregnancy-related), barbiturates, valproic acid, phenytoin, and exogenous glucocorticoids may cause impaired response to metyrapone.

There have been occasional reports of Addisonian crisis during 2-day metyrapone testing. For this reason, 2-day metyrapone testing probably should not be performed when plasma cortisol values are less than 3 mcg/dL.

Clinical Reference


Performance

Method Description
The specimen and an internal standard are assayed by liquid chromatography-tandem mass spectrometry. The analyte is detected by multiple-reaction monitoring. (Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Tuesday; 10 a.m.

Analytic Time
3 days

Maximum Laboratory Time
9 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
82634

LOINC® Information

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<tbody>
<tr>
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<td>11-Deoxycortisol, S</td>
<td>1657-6</td>
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<table>
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<th>Test Result Name</th>
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<tbody>
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