Overview

Useful For
Differential diagnosis and follow-up of patients with urea cycle disorders

Highlights
Urea cycle disorders (UCD) are a group of inherited disorders of nitrogen detoxification that result from defects in any of the enzymes involved in the urea cycle.

Disruption of the urea cycle can result in the accumulation of ammonia which is toxic to the nervous system.

Plasma amino acid analysis can be used to aid in the diagnosis of a UCD as well as for follow-up of a known patient.

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

NY State Available
Yes

Specimen

Specimen Type
Plasma

Necessary Information
1. Patient's age is required.

2. Include family history, clinical condition (asymptomatic or acute episode), diet, and drug therapy information.

Specimen Required
Patient Preparation: Fasting (overnight preferred, 4 hours minimum). Infants should be drawn just before next feeding (2-3 hours without total parenteral nutrition if possible).

Collection Container/Tube:

Preferred: Green top (sodium heparin)

Acceptable: Lavender top (EDTA) or green top (lithium heparin)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Collection Instructions:

1. Centrifuge within 4 hours if specimen is stored at refrigerated temperature and aliquot plasma.

2. Send plasma frozen.
Forms
If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume
0.25 mL

Reject Due To
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<th>OK</th>
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<tr>
<td>Gross lipemia</td>
<td>OK</td>
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<tr>
<td>Gross icterus</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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<tbody>
<tr>
<td>Plasma</td>
<td>Frozen</td>
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Clinical and Interpretive

Clinical Information
Urea cycle disorders (UCD) are a group of inherited disorders of nitrogen detoxification that result when any of the enzymes in the urea cycle (carbamoylphosphate synthetase I: CPS I; ornithine transcarbamylase: OTC; argininosuccinic acid synthetase; argininosuccinic acid lyase; arginase; or the cofactor producer, N-acetyl glutamate synthetase: NAGS), have deficient or reduced activity. The role of the urea cycle is to metabolize and clear waste nitrogen, and defects in any of the steps of the pathway can result in an accumulation of ammonia, which can be toxic to the nervous system. The urea cycle is also responsible for endogenous production of the amino acids citrulline, ornithine, and arginine. Infants with a complete urea cycle enzyme deficiency typically appear normal at birth, but present with in the neonatal period as ammonia levels rise with lethargy, seizures, hyper- or hypoventilation, and ultimately coma or death. Individuals with partial enzyme deficiency may present later in life, typically following an acute illness or other stressor. Symptoms may be less severe and may present with episodes of psychosis, lethargy, cyclical vomiting, and behavioral abnormalities. Patients with impaired ornithine metabolism due to ornithine aminotransferase (OAT) deficiency may present with childhood onset myopia progressing to vision loss in the 4th to 6th decades of life. Patients may or may not have accompanying hyperammonemia, but display marked elevations in plasma ornithine.

All of the UCD are inherited as autosomal recessive disorders, with the exception of OTC deficiency, which is X-linked. UCD may be suspected with elevated ammonia, normal anion gap, and a normal glucose. Plasma amino acids can be used to aid in the diagnosis of UCD and may aid in monitoring treatment effectiveness. Measurement of urinary orotic acid, enzyme activity (CPS I, OTC, or NAGS), and molecular genetic testing can help to distinguish the conditions and allows for diagnostic confirmation.

Acute treatment for UCD consists of dialysis and administration of nitrogen scavenger drugs to reduce ammonia concentration. Chronic management typically involves restriction of dietary protein with essential amino acid supplementation. More recently, orthotopic liver transplantation has been used with success in treating some patients.
Reference Values

GLUTAMINE

&lt; or =23 months: 316-1020 nmol/mL
2-17 years: 329-976 nmol/mL
&gt; or =18 years: 371-957 nmol/mL

ORNITHINE

&lt; or =23 months: 20-130 nmol/mL
2-17 years: 22-97 nmol/mL
&gt; or =18 years: 38-130 nmol/mL

CITRULLINE

&lt; or =23 months: 9-38 nmol/mL
2-17 years: 11-45 nmol/mL
&gt; or =18 years: 17-46 nmol/mL

ARGININE

&lt; or =23 months: 29-134 nmol/mL
2-17 years: 31-132 nmol/mL
&gt; or =18 years: 32-120 nmol/mL

ARGINOSUCCINIC ACID

&lt;2 nmol/mL

Reference value applies to all ages.

Interpretation

The quantitative results of glutamine, ornithine, citrulline, arginine, and argininosuccinic acid with age-dependent reference values are reported without added interpretation. When applicable, reports of abnormal results may contain an interpretation based on available clinical interpretation.

Cautions

Reference values are for fasting patients.

Clinical Reference

Test Definition: AAUCD
Amino Acid, Urea Cycle Panel, P


Performance

Method Description
Quantitative analysis of amino acids is performed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) by labeling amino acids present in plasma, urine, and spinal fluid with aTRAQ Reagent 121. Samples are dried and reconstituted with aTRAQ Reagent 113-labeled Standard Mix. Amino acids are separated and detected by LC-MS/MS. The concentrations of amino acids are established by comparison of their ion intensity (121-labeled amino acids) to that of their respective internal standards (113-labeled amino acids). (Lacey JM, Casetta B, Daniels SB, et al: Quantitation in plasma, urine and CSF by iTRAQ reagent amino acid analysis kit and MS-MS. J Am Soc Mass Spectrom 2008;19[5]:S97)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 9 a.m. and 1 p.m.

Analytic Time
3 days (not reported on Saturday or Sunday)

Maximum Laboratory Time
5 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
Test Definition: AAUCD
Amino Acid, Urea Cycle Panel, P

- 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
82136

LOINC® Information

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