Overview

Useful For
Evaluation of the differential diagnosis of hyperammonemia and hereditary orotic aciduria
Sensitive indicator of ornithine transcarbamylase (OTC) activity after administration of allopurinol or a protein load to identify OTC carriers

Special Instructions
- Biochemical Genetics Patient Information

Method Name
Colorimetric

NY State Available
Yes

Specimen

Specimen Type
Urine

Necessary Information
1. Patient's age is required.
2. Provide a reason for testing.

Specimen Required
Supplies: Urine Tubes, 10 mL (T068)
Container/Tube: Plastic, 10-mL urine tube
Specimen Volume: 10 mL
Collection Instructions:
1. Collect a random or timed urine specimen.
2. No preservative.

Forms
1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Minimum Volume
3 mL
Test Definition: OROT
Orotic Acid, U

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>Frozen (preferred)</td>
<td>30 days</td>
<td></td>
</tr>
</tbody>
</table>

Clinical & Interpretive

Clinical Information
Urinary excretion of orotic acid, an intermediate in pyrimidine biosynthesis, is increased in many urea cycle disorders and in a number of other disorders involving the metabolism of arginine. The determination of orotic acid can be useful to distinguish between various causes of elevated ammonia (hyperammonemia). Hyperammonemia is characteristic of all urea cycle disorders, but orotic acid is elevated in only some, including ornithine transcarbamylase (OTC) deficiency, citrullinemia, and argininosuccinic aciduria. Orotic acid is also elevated in the transport defects of dibasic amino acids (lysinuric protein intolerance and hyperornithinemia, hyperammonemia, and homocitrullinuria [HHH] syndrome) and is greatly elevated in patients with hereditary orotic aciduria (uridine monophosphate synthase [UMPS] deficiency).
OTC deficiency is an X-linked urea cycle disorder that affects both male patients and, due to random X-inactivation, female patients. It is thought to be the most common urea cycle disorder with an estimated incidence of 1:56,000. In OTC deficiency, carbamoyl phosphate accumulates and is alternatively metabolized to orotic acid. Allopurinol inhibits orotidine monophosphate decarboxylase and, when given to OTC carriers (who may have normal orotic acid excretion), can cause increased excretion of orotic acid. When orotic acid is measured after a protein load or administration of allopurinol, its excretion is a very sensitive indicator of OTC activity. A carefully monitored allopurinol challenge followed by several determinations of a patient’s orotic acid excretion can be useful to identify OTC carriers, as approximately 20% of OTC variant are not detectable by current molecular genetic testing methods.

Reference Values
<2 weeks: 1.4-5.3 mmol/mol creatinine
2 weeks-1 year: 1.0-3.2 mmol/mol creatinine
2-10 years: 0.5-3.3 mmol/mol creatinine
> or =11 years: 0.4-1.2 mmol/mol creatinine

Interpretation
The value for the orotic acid concentration is reported. The interpretation of the result must be correlated with clinical and other laboratory findings.

Cautions
Pregnant women will normally excrete up to twice the upper limit of the adult reference range.

Clinical Reference
Test Definition: OROT
Orotic Acid, U


Performance

Method Description
Interfering substances such as amino acids, urea, pigments, and creatinine are removed from the urine by passing it through a cation-exchange resin. The orotic acid is then brominated to form dibromobarbituric acid, reduced to barbituric acid with ascorbic acid, and finally condensed with dimethylaminobenzaldehyde to form 5(p-dimethylaminobenzaldehyde)-barbituric acid. The absorbance of the final product is measured at 480 nm using a control reaction as reference. (Harris ML, Oberholzer VG: Conditions affecting the colorimetry of orotic acid and orotidine in urine. Clin Chem. 1980;26[3]:473-479); Cowan T, Pasquali M: Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

PDF Report
No

Specimen Retention Time
1 month

Performing Laboratory Location
Rochester

Fees & Codes

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 US Food and Drug Administration.

CPT Code Information
83921