

## 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 referral.

### 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) in Special Instructions.
2. If not ordering electronically, complete, print, and send an [Inborn Errors of Metabolism Test Request](#) (T798) with the specimen.

### Specimen Minimum Volume

3 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	Frozen	30 days	

**Clinical and 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**

1. Singh RH, Rhead WJ, Smith W, et al: Nutritional management of urea cycle disorders. *Crit Care Clin* 2005 Oct;21(4 Suppl):S27-35
2. Lee B, Singh RH, Rhead WJ, et al: Considerations in the difficult-to-manage urea cycle disorder patient. *Crit Care Clin* 2005 Oct;21(4 Suppl):S19-25
3. Brusilow SW, Horwich AL: Urea Cycle Enzymes. In *The Online Metabolic and Molecular Bases of Inherited Disease*. Edited by D Valle, S Antonarakis, A Ballabio, et al. McGraw-Hill. Accessed 1/13/2020. Available at <http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225084071>
4. Webster DR, Becroft DO, van Gennip AH, Van Kuilenburg AP: Hereditary Orotic Aciduria and Other Disorders of Pyrimidine Metabolism. In *The Online Metabolic and Molecular Bases of Inherited Disease*. Edited by D Valle, S Antonarakis, A Ballabio, et al. , McGraw-Hill. Accessed 1/13/2020. Available at <http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225090376>
5. Ah Mew N, Simpson KL, Gropman AL, et al: Urea Cycle Disorders Overview. In *GeneReviews*. Edited by MP Adam, HH Ardinger, RA Pagon, et al. University of Washington, Seattle, 1993-2020. Updated 2017 Jun 22. Accessed 1/13/2020. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK1217>

## 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 *Pediatric Endocrinology and Inborn Errors of Metabolism*. Second Edition. Edited by K Sarafoglou, GF Hoffman, KS Roth. 2017, pp 1139-1158)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Wednesday; 8 a.m.

### Analytic Time

8 days

### Maximum Laboratory Time

15 days

### Specimen Retention Time

1 month

### Performing Laboratory Location

Rochester

## Fees and Codes

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**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**

83921

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
OROT	Orotic Acid, U	17869-9

Result ID	Test Result Name	Result LOINC Value
8905	Orotic Acid, U	17869-9