# Orotic Acid and Orotidine

*FOR PATIENTS WITH A SUSPECTED UREA CYCLE DISORDER, UNEXPLAINED HYPERAMMONEMIA, OR SUSPECTED HEREDITARY OROTIC ACIDURIA*

## Disease Overview

- Orotic acid may be elevated in patients with urea cycle disorders, hereditary orotic aciduria, and other causes of elevated ammonia.
- The urea cycle is the body's primary system for removing waste nitrogen produced by the metabolism of protein and other nitrogen-containing molecules. Defects in the urea cycle can lead to life-threatening accumulations of ammonia. Several enzymes, each encoded by a different gene, are involved in the urea cycle; mutations in any of the urea cycle genes may cause a urea cycle defect.
  - Classic urea cycle disorders are characterized by hyperammonemia, cyclical vomiting, seizures, lethargy, coma, and neonatal death if not treated.
  - Elevated levels of orotic acid appear in many urea cycle disorders, including ornithine transcarbamylase (OTC) deficiency, citrullinemia type I, argininosuccinate lyase deficiency, arginase deficiency, lysinuric protein intolerance, and hyperornithinemia-hyperammonemia-homocitrullinemia.
- Hereditary orotic aciduria is a rare condition caused by deficiency of the enzyme uridine-5-monophosphate. Symptoms include megaloblastic anemia, neutropenia, crystalluria, and susceptibility to infection.

## Epidemiology

- Incidence of urea cycle disorders is approximately one in 25,000 overall but may be higher due to partial deficiencies.
- Hereditary orotic aciduria is very rare.

## Genetics

- Most urea cycle disorders are autosomal recessive; OTC is X-linked.
- Hereditary orotic aciduria is autosomal recessive.

## Indications for Ordering

- In patients with elevated ammonia, initial testing often includes plasma amino acids (AA) and urine organic acids (OA).
- Orotic acid testing may be ordered subsequent to or in conjunction with testing for AA and OA.

## Contraindications for Ordering

- Not recommended as a stand-alone test to evaluate patients with hyperammonemia.
- This test will not determine carrier status.

## Methodology

- Liquid chromatography/tandem mass spectrometry to quantify orotic acid and orotidine.
- Standard orotic acid methodologies do not separate orotidine and orotic acid.
- Separation of orotidine from orotic acid by ARUP's test allows for more precise orotic acid measurement.

## Interpretation

- Normal concentrations of orotic acid and orotidine do not exclude a urea cycle disorder.
- Other disorders causing hyperammonemia may also show elevated orotic acid levels.
- Pregnant women may have higher-than-normal ortic acid excretion.

## Limitations

- This test cannot predict disease severity.
- This test cannot determine carrier status.

## Related Tests

- 0080710 Amino Acids Quantitative, Plasma
- 0098389 Organic Acids, Urine
- 2004896 Ornithine Transcarbamylase Deficiency (OTC) Sequencing and Deletion/Duplication

## References

1. Lanpher BC, et al. Urea cycle disorders overview. GeneReviews. http://www.ncbi.nlm.nih.gov/books/NBK1217/. Accessed October 18, 2011.
2. Summar ML. Urea cycle disorders. In: Sarafoglou K, Hoffman GF, Roth KS, eds. *Pediatric Endocrinology and Inborn Errors of Metabolism*. New York, NY: McGraw-Hill; 2009a:141–152.
3. Salerno C, Crifo C. Diagnostic value of urinary orotic acid levels: applicable separationmethods. *J Chromatogr.* 2002;781:57–71.
4. Brusilow SW, Horwich AL. Urea cycle enzymes. In: Scriver CR, et al., eds. *The Metabolic and Molecular Bases of Inherited Disease*. 8th ed. New York, NY: McGraw-Hill; 2001:1916–1925.



500 Chipeta Way, Salt Lake City, UT 84108 | (800) 522-2787 | (801) 583-2787 | www.aruplab.com | www.arupconsult.com

## Test Information

**0092458 Orotic Acid and Orotidine, Urine**

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.
For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.


## AUTHORS

Amanda Openshaw, MS, LCGC
Marzia Pasquali, PhD
Nicola Longo, MD, PhD