

Organic Acids, Urine

Background

Organic acids refer to a family of compounds that are intermediates in a variety of metabolic pathways. Many organic acids are present in urine from clinically normal individuals. Elevated levels of specific organic acids or elevations of combinations of specific organic acids are often seen in the organic acidurias, disorders in which one or more metabolic pathways of organic acid metabolism are blocked. Abnormal urinary organic acids are also seen in some disorders of amino acid metabolism, some disorders of mitochondrial fatty acid beta-oxidation, and some disorders of mitochondrial oxidative phosphorylation. All of these disorders are genetic conditions. Abnormal urinary organic acids can also be seen in certain pathologic, non-genetic states such as ketosis associated with starvation or diabetes and some types of renal dysfunction. An analysis of urinary organic acids is usually a key test in the evaluation of patients with a suspected genetic disorder of organic acid metabolism and is frequently used in the evaluation of persons with possible genetic disorders of mitochondrial fatty acid metabolism, amino acid disorders, and disorders of mitochondrial oxidative phosphorylation.

Disorders of organic acid metabolism have various clinical presentations and ages of onset. Common presentations include an acute life-threatening illness in early infancy or unexplained developmental delay with intercurrent episodes of metabolic decompensation in later childhood. Clinical presentations in the teenage years or even later are also described.

The mitochondrial fatty acid beta-oxidation disorders and disorders of mitochondrial oxidative phosphorylation can similarly present very early in life, in childhood, or in the adult years. Some of the common presentations include lethargy, fasting intolerance, myalgias, myopathy, exercise intolerance, cardiomyopathy and various types of developmental or neurological disability such as seizures or vision deficit.

Clinical Indications

Some of the common [clinical indications](#) for ordering a urinary organic acid analysis include evaluation of:

- neonates and infants with an unexplained life-threatening phenotype
- infants, children and selected adults with unexplained cognitive disability or developmental regression
- infants, children and selected adults with unexplained epilepsy
- any age individual with unexplained intermittent encephalopathy
- infants, children and selected adults with two or more unexplained CNS handicaps
- infants, children and selected adults with unexplained growth retardation or failure to thrive
- any age individual with unexplained fasting intolerance
- any age individual with unexplained exercise intolerance.

Some of the common [clinical laboratory indications](#) for ordering a urinary organic acid analysis include evaluation of:

- neonates with unexplained moderate or marked ketonuria
- neonates, infants, children and selected adults with unexplained anion gap acidosis
- neonates, infants, children and selected adults with unexplained hyperammonemia
- neonates, infants, children and selected adults with unexplained hypoglycemia
- neonates, infants, children and selected adults with unexplained lactic acidemia

In general, the genetic disorders detected by urinary organic acid analysis present at some time during infancy or childhood, often in the context of significant catabolic stresses such as an illness with vomiting, diarrhea and/or fever or fasting. Presentations during young adult years are also often prompted by illness, fasting or marked exercise and are commonly intermittent.

Results and/or Interpretation

The interpretation of the urinary organic acid analysis is based on: (1) age-related levels of the urinary organic acids; (2) patterns of the abnormally elevated organic acids; and (3) any pertinent negative findings (for example, the absence of an elevated urinary level of certain organic acids in the context of others that are elevated).

An abnormal urinary organic acid analysis is usually not sufficient to conclusively establish a diagnosis of a particular genetic metabolic disorder. We strongly recommend having

additional confirmatory testing. The latter is often done using enzyme-based assays (of blood, cultured cells, tissue biopsy) or by molecular genetic analysis of particular genes. The choice of confirmatory assay depends on the particular disorder that is suspected.

Methodology

The urinary organic acids are extracted from urine by organic solvent extraction and then identified and quantified by gas chromatography-mass spectrometry.

Test Overview

Test Name	Organic Acids, Urine
Ordering Mnemonic	UORGSC
Methodology	Gas chromatography-mass spectrometry
Specimen Requirements	10 mL random urine, no preservative; minimum volume 3 mL
Clinical Information	Indicate clinical condition and reason for testing, diet and/or drug therapy information (if applicable), and family history information (if relevant). Age of patient or date of birth required. Stability: frozen (preferred) for 90 days; 24 hours refrigerated; ambient 2 hours. Urine samples from outside Cleveland Clinic must be sent frozen (on dry ice).
Billing Code	76978
CPT Code	83919(x1)

Technical Information Contact:

Chao Yuan, PhD
216.444.1004
yaunc@ccf.org

Scientific/Medical Information Contact:

Marvin Natowicz, MD, PhD
216.445.3735
natowim@ccf.org