

Organic Acid Disorders (NBS)

Use

Quantitative measurement of free carnitine and acylcarnitines in blood specimens dried on filter paper as an aid in screening newborns for organic acid disorders, including propionic acidemia (PROP), methylmalonic acidemia (MUT; CBL-C,D; CBL- A,B), malonic acidemia (MAL), isobutyrylglycinuria (IBG), isovaleric acidemia (IVA), 2-methylbutyrylglycinuria (2MBG), 3-methylcrotonyl-CoA carboxylase deficiency (3MCC), 3- methylglutaconic aciduria (3MGA), 3-hydroxy-3-methylglutaric aciduria (HMG), holocarboxylase synthetase deficiency (MCD), 2-methyl- 3hydroxybutyric aciduria (2M3HBA), beta-ketothiolase deficiency (BKT), and glutaric acidemia type 1 (GA1).

Clinical Significance

Elevated or decreased free carnitine and elevated acylcarnitine levels in newborn blood can be indicative of one or more metabolic disorders, generally classified as fatty acid oxidation (FAO) and organic aciduria or acidemia (OA) disorders. These rare disorders are inborn errors of metabolism (or genetic metabolic deficiencies). OA disorders are characterized by the accumulation of abnormal (usually toxic) organic acid metabolites in the blood, urine, and other body fluids, and primarily result from enzyme deficiencies in the breakdown pathways of amino acids. Most OAs become clinically apparent during the newborn period or early infancy, although there are milder forms that may not present until adolescence or adulthood or may never come to medical attention. Resulting modifications or adaptations to intermediary metabolic pathways may cause variable clinical symptoms, including metabolic acidosis, ketosis, hyperammonemia, failure to thrive, sepsis or coma. After an initial period of well-being, affected individuals develop a life-threatening episode of metabolic acidosis. This presenting episode may be mistaken for sepsis and, if unrecognized, is associated with significant mortality. Metabolic decompensation can occur during episodes of increased catabolism, such as intercurrent illness, trauma, surgery, or prolonged episodes of fasting. Further information and ACT Sheets can be found at the OSDH Newborn Screening Program [website](#).

Methodology

Flow Injection-Tandem mass spectrometry (FIA-MS/MS)

Specimen Type

See [Guidance for Collection of NBS Dried Blood Spots](#)

Minimum Volume/Size

See [Guidance for Collection of NBS Dried Blood Spots](#)

Collection Instructions

See [Guidance for Collection of NBS Dried Blood Spots](#)

Common Causes for Rejection

See [Guidance for Collection of NBS Dried Blood Spots](#)

Shipping

See [Guidance for Collection of NBS Dried Blood Spots](#)

Turn-around Time

Within 5 working days of receipt

Reference Range

- C3 < 8.20 $\mu\text{mol/L}$
- C3DC < 0.44 $\mu\text{mol/L}$
- C4 < 1.27 $\mu\text{mol/L}$
- C5 < 0.87 $\mu\text{mol/L}$
- C5:1 < 0.10 $\mu\text{mol/L}$
- C5DC < 0.46 $\mu\text{mol/L}$
- C5OH_C4DC < 0.80 $\mu\text{mol/L}$
- C6DC < 0.27 $\mu\text{mol/L}$
- C3/C2 ratio < 0.30
- C5/C2 ratio < 0.05
- C5DC/C8 ratio < 7.64
- C5DC/C16 ratio < 0.66

Reportable Results

- Within Normal Limits
- Outside Normal Limits

Interpretation

- Within Normal Limits
 - Not consistent with Organic Acid Disorders
- Outside Normal Limits
 - Elevated: Submit repeat specimen as soon as possible
 - Repeat Elevated: Possible <OA disorder>; immediate confirmatory testing recommended
 - High: Consistent with <OA disorder>; immediate confirmatory testing recommended
 - Pattern of Multiple Elevations: Acylcarnitine pattern consistent with high nutritional intake of carnitine and/or MCT oil; submit new specimen at 14 days of age

Limitations/Interferences

- This is a screening test only. A diagnostic procedure should be used for confirmation of presumptive abnormal acylcarnitines profiles.
- Pivalic acid (an antibiotic that may be administered during pregnancy or to the infant) may result in false positive cases for IVA.
- High nutritional intake of carnitine or medium-chain triglyceride (MCT) oil may interfere with the validity of acylcarnitines concentrations.
- Variables such as hematocrit, prematurity, and age of infant may affect the interpretation of the values produced.
- Specimens improperly collected, processed or transported may result in erroneous results.

CPT Code

82017 (includes MCAD and other fatty acid oxidation disorders)

Notes

This test is approved for *in vitro* diagnostic use by the U.S. Food and Drug Administration.