

Overview

Useful For

Evaluation of patients with an abnormal newborn screen showing elevations of glutarylcarnitine (C5-DC)

Evaluation of patients with abnormal newborn screens showing elevations of C4-acylcarnitine to aid in the differential diagnosis of short-chain acyl-CoA dehydrogenase and isobutyryl-CoA dehydrogenase deficiencies

Diagnosis of glutaric acidemia type 1

Aids in diagnosis of glutaric acidemia type 2

Genetics Test Information

Second-tier newborn screening for follow-up of C4-acylcarnitine and glutarylcarnitine (C5DC) elevations.

Differentiating diagnoses of short-chain Co-A dehydrogenase (SCAD) deficiency, isobutyryl-CoA dehydrogenase (IBDH) deficiency, and ethylmalonic encephalopathy.

Differentiating diagnoses of glutaric acidemia type I (GA-1) and glutaric acidemia type II (GA-2)

Special Instructions

- [Biochemical Genetics Patient Information](#)
- [Blood Spot Collection Card-Spanish Instructions](#)
- [Blood Spot Collection Card-Chinese Instructions](#)
- [Blood Spot Collection Instructions](#)

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Card-Blood Spot Collection (Filter Paper) (T493) from heel or finger stick

Acceptable: Ahlstrom 226 filter paper, Munktell filter paper, Whatman Protein Saver 903 paper, available newborn screening card, blood collected in tubes containing heparin or EDTA and dried on filter paper

Specimen Volume: 2 blood spots

Collection Instructions:

1. Do not use device or capillary tube containing ACD to collect specimen. Sodium heparin or EDTA are acceptable, but must be spotted on card the same day as collected.
2. Completely fill at least 2 circles on the filter paper card (approximately 100 microliters blood per circle).
3. Let blood dry on filter paper at room temperature in a horizontal position for 3 or more hours.
4. Do not stack wet specimens.
5. Do not expose specimen to heat or direct sunlight.
6. Keep specimen dry.

Additional Information:

1. For collection instructions, see [Blood Spot Collection Instructions](#) in Special Instructions.
2. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777) in Special Instructions.
3. For collection instructions in Chinese, see [Blood Spot Collection Card-Chinese Instructions](#) (T800) in Special Instructions.

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

Blood spot: 1

Reject Due To

Blood spot	Shows serum rings Insufficient specimen Blood collected with ACD Nonapproved filter paper
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Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	123 days	FILTER PAPER
	Frozen	123 days	FILTER PAPER
	Refrigerated	123 days	FILTER PAPER

Clinical and Interpretive

Clinical Information

Acylcarnitine analysis is included in newborn screening blood testing and is utilized for detection of several inborn errors of metabolism, including fatty acid oxidation disorders (FAOD) and organic acidemias (OA). A limitation of this analytic method is its inability to differentiate between several isomers. Additional testing of 2-hydroxy glutaric acid (2OH-GA), 3-hydroxy glutaric acid (3OH-GA), glutaric acid (GA), methylsuccinic acid (MSA), and ethylmalonic acid (EMA) by LC-MS/MS allows better differentiation among C4-acylcarnitine and glutarylcarnitine/C10-OH isomers.

C4-acylcarnitine represents both butyrylcarnitine and isobutyrylcarnitine and is elevated in short-chain acyl Co-A dehydrogenase (SCAD) deficiency, isobutyryl-CoA dehydrogenase (IBDH) deficiency, and ethylmalonic encephalopathy (EE). SCAD deficiency is a condition affecting fatty acid metabolism, with reported symptoms of hypoglycemia, lethargy, developmental delays, and failure to thrive. There is controversy on whether a biochemical diagnosis necessarily confers clinical symptoms. IBDH deficiency is characterized by cardiomyopathy, hypotonia, and developmental delays, although many individuals with IBDH deficiency are asymptomatic. EE is a rare progressive encephalopathy associated with hypotonia, seizures, and abnormal movements.

Individuals with SCAD deficiency demonstrate elevated plasma EMA and MSA levels and individuals with EE show only elevations in EMA, while individuals with IBDH deficiency do not typically have elevations in either EMA or MSA.

Glutarylcarnitine (C5-DC) is elevated in glutaric acidemia type 1 (GA-1), but is not differentiated from C10-OH acylcarnitine. GA-1, is caused by a deficiency of glutaryl-CoA dehydrogenase and is characterized by bilateral striatal brain injury leading to dystonia, often a result of acute neurologic crises triggered by illness. Individuals with GA-1 typically show elevations of glutaric acid and 3OH-GA, even in those considered to be "low excretors."

Glutaric acidemia (GA-2), also known as multiple acyl-CoA dehydrogenase deficiency (MADD), is caused by defects in either the electron transfer flavoprotein (ETF) or ETF-ubiquinone oxidoreductase. This disease can be severe and is often fatal in the first weeks of life, with typical symptoms of hypoglycemia, muscle weakness, metabolic acidosis, dysmorphic features, cardiac defects or arrhythmias, renal cysts, and fatty infiltration of the liver. GA-2 can have a milder presentation, also known as ethylmalonic-adipic aciduria, with Reye-like illnesses in childhood and muscle weakness in childhood and adulthood. In addition to elevations in glutaric acid, individuals with GA-2 can also show increased EMA, MSA, and 2OH-GA.

The American College of Medical Genetics (ACMG) newborn screening work group published diagnostic algorithms for the follow-up of infants who had a positive newborn screening result. For more information, see www.acmg.net.

Reference Values

2-OH Glutaric acid: < or =25 nmol/mL

3-OH Glutaric acid: < or =1.5 nmol/mL

Glutaric acid: < or =1.5 nmol/mL

Methylsuccinic acid: < or =0.45 nmol/mL

Ethylmalonic acid: < or =3.5 nmol/mL

Interpretation

[Elevations of ethylmalonic acid \(EMA\) and methylsuccinic acid \(MSA\) are consistent with a diagnosis of short-chain acyl Co-A dehydrogenase \(SCAD\) deficiency.](#)

Elevation of EMA is consistent with a diagnosis of ethylmalonic encephalopathy.

Normal levels of EMA in the context of elevated C4 is consistent with a diagnosis of isobutyryl-CoA dehydrogenase (IBDH) deficiency.

Elevation of glutaric acid (GA) and 3-hydroxy glutaric acid (3OH-GA) are consistent with a diagnosis of glutaric acidemia type 1 (GA-1).

Elevation of GA, 2-hydroxy glutaric acid (2OH-GA), 3OH-GA, EMA, and MSA are consistent with a diagnosis of glutaric acidemia (GA-2).

Cautions

No significant cautionary statements

Clinical Reference

1. Rinaldo P, Cowan TM, Matern D: Acylcarnitine profile analysis. 2008;10(2):151-156
2. Kolker S, Christensen E, Leonar JV, et al: Diagnosis and management of glutaric aciduria type I-revised recommendations. J Inherit Metab Dis 2011;34:677-694
3. Frerman FE, Goodman SI: Chapter 103: Defects of electron transfer flavoprotein and electron transfer flavoprotein-ubiquinone oxidoreductase: Glutaric Acidemia Type II. In Scriver's Online Metabolic and Molecular Bases of Inherited Disease. Edited by CR Scriver, AL Beaudet, D Valle, et al. Accessed 8/17/17. Available at www.ommbid.com/

Performance

Method Description

Internal standard is added to a dried blood spot. The extract is evaporated and reconstituted prior to injection onto aliquid chromatography-tandem mass spectrometry (LC-MS/MS) system. The ratios of the extracted peak areas of glutaric acid (GA), ethylmalonic acid (EMA), and methylsuccinic acid (MSA) to their respective internal standards as determined by LC-MS/MS are used to calculate the concentration of each analyte in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday, Wednesday; 8 a.m.

Analytic Time

2 days

Maximum Laboratory Time

10 days

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

Fees and Codes

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

83918

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HGEM	HGEM, BS	92672-5

Result ID	Test Result Name	Result LOINC Value
36048	2-OH Glutaric acid	75037-2
36049	3-OH Glutaric acid	82505-9
36050	Glutaric acid	82504-2
36051	Methylsuccinic acid	82503-4
36052	Ethylmalonic acid	82502-6
36053	Interpretation (HGEM)	59462-2
36054	Reviewed By	18771-6