

Overview

Useful For

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

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

Aiding 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 acyl-CoA 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)

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Plasma

Necessary Information

Patient's age is required.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Collection Container/Tube:

Preferred: Green top (sodium heparin)

Acceptable: Lavender top (EDTA), green top (lithium heparin)
Submission Container/Tube: Plastic vial
Specimen Volume: 0.1 mL
Collection Instructions: Centrifuge and aliquot plasma into a plastic vial.

Forms
[If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request](#) (T798) with the specimen.

Specimen Minimum Volume
0.02 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Ambient	12 days	
	Refrigerated (preferred)	90 days	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Acylcarnitine analysis is included in newborn screening blood tests 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-hydroxyglutaric acid (2OH-GA), 3-hydroxyglutaric acid (3OH-GA), glutaric acid (GA), methylsuccinic acid (MSA), and ethylmalonic acid (EMA) by liquid chromatography tandem mass spectrometry allows better differentiation among C4 acylcarnitine and glutaryl-carnitine/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.

Glutarylcarntine (C5-DC) is elevated in glutaric acidemia type I (GA1) but is not differentiated from C10-OH acylcarnitine. GA1 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 GA1 typically show elevations of GA and 3OH-GA, even in those considered to be "low excretors."

Glutaric acidemia type II (GA2), 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. GA2 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 GA, individuals with GA2 can also show increased EMA, MSA, and 2OH-GA.

The American College of Medical Genetics and Genomics 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 =4.5 nmol/mL

3-OH Glutaric acid < or =0.7 nmol/mL

Glutaric acid < or =0.8 nmol/mL

Methylsuccinic acid < or =0.3 nmol/mL

Ethylmalonic acid < or =1.5 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-hydroxyglutaric acid (3OH-GA) are consistent with a diagnosis of glutaric acidemia type I (GA1).

Elevation of GA, 2-hydroxyglutaric acid (2OH-GA), 3OH-GA, EMA, and MSA are consistent with a diagnosis of glutaric acidemia type II (GA2).

Cautions

No significant cautionary statements

Clinical Reference

1. Rinaldo P, Cowan TM, Matern D. Acylcarnitine profile analysis. Genet Med. 2008;10(2):151-156
2. Vockley J, Zschocke J, Knerr I, Vockley C, Michael Gibson KK. Branched chain organic acidurias. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed April 1, 2025. Available at <https://ommbid.mhmedical.com/content.aspx?bookid=2709§ionid=225085758>
3. Frerman FE, Goodman SI. Defects of electron transfer flavoprotein and electron transfer flavoprotein-ubiquinone oxidoreductase: Glutaric acidemia type II. n: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed April 1, 2025. Available at <https://ommbid.mhmedical.com/content.aspx?bookid=2709§ionid=225088261>
4. Larson A, Goodman S. Glutaric acidemia type 1. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2019. Accessed April 1, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK546575/
5. Di Meo I, Lamperti C, Tiranti V. Ethylmalonic encephalopathy. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2017. Accessed April 1, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK453432/
6. Wolfe L, Jethva R, Oglesbee D, Vockley J. Short-chain acyl-CoA dehydrogenase deficiency. In: Adam MP, Mirzaa GM, Pagon RA, et al. eds. GeneReviews [Internet]. University of Washington, Seattle; 2011. Updated August 9, 2018. Accessed April 1, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK63582/

Performance

Method Description

An aqueous internal standard is added to the specimen. The supernatant is evaporated under heated nitrogen, and the residue is then reconstituted prior to injection onto a liquid chromatography tandem mass spectrometry (LC-MS/MS). The ratios of the extracted peak areas of glutaric acid, ethylmalonic acid, and methylsuccinic acid 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) Performed

Monday, Wednesday

Report Available

3 to 7 days

Specimen Retention Time

2 months

Performing Laboratory Location
Rochester

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

83918

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HGEMP	HGEM, P	92673-3

Result ID	Test Result Name	Result LOINC® Value
36063	3-OH Glutaric acid	69851-4
36062	2-OH Glutaric acid	69845-6
36064	Glutaric acid	27301-1
36065	Methylsuccinic acid	69829-0
36066	Ethylmalonic acid	79476-8
36067	Interpretation (HGEMP)	59462-2
36068	Reviewed By	18771-6