Test Definition: C5OHU

C5-OH Acylcarnitine, Quantitative, Random, Urine

Overview

Useful For
Evaluation of patients with an abnormal newborn screen showing elevations of 3-hydroxyisovaleryl-/2-methyl-3-hydroxybutyryl-carnitine

Genetics Test Information
Elevated 3-hydroxyisovaleryl-/2-methyl-3-hydroxy acylcarnitine (C5-OH) in plasma or newborn screening blood spots is due to one of several biochemical genetic diagnoses: 3-methylcrotonylglycinuria, 3-hydroxy 3-methylglutaryl-CoA lyase deficiency, beta-ketothiolase deficiency, 2-methyl 3-hydroxybutyryl-CoA dehydrogenase deficiency, 3-methylglutaconic aciduria, biotinidase deficiency or holocarboxylase deficiency.

Urine C5-OH is useful in differentiating patients with 3-methylcrotonylglycinuria and with 3-methylglutaconic aciduria as they typically excrete larger amounts of C5-OH in urine compared to patients with the other diagnoses.

Highlights
Elevated 3-hydroxyisovaleryl-/2-methyl-3-hydroxy acylcarnitine (C5-OH) in plasma or newborn screening blood spots is due to one of several biochemical genetic diagnoses: 3-methylcrotonylglycinuria, 3-hydroxy 3-methylglutaryl-(HMG)-CoA lyase deficiency, beta-ketothiolase deficiency, 2-methyl 3-hydroxybutyryl-CoA dehydrogenase deficiency, 3-methylglutaconic aciduria, biotinidase deficiency or holocarboxylase deficiency.

Urine C5-OH is useful in differentiating patients with 3-methylcrotonylglycinuria and with 3-methylglutaconic aciduria as they typically excrete larger amounts of C5-OH in urine compared to patients with the other diagnoses.

Method Name
Flow Injection Analysis-Tandem Mass Spectrometry (FIA-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Urine

Ordering Guidance
This second-tier test is used specifically to evaluate a newborn screening elevation of 3-hydroxyisovaleryl-/2-methyl-3-hydroxy acylcarnitine and **must not** be ordered with either C4U / C4 Acylcarnitine, Quantitative, Random, Urine or C5DCU / C5-DC Acylcarnitine, Quantitative, Random, Urine.

Test Definition: C5OHU

C5-OH Acylcarnitine, Quantitative, Random, Urine

For general screening for metabolic disorders, see OAU / Organic Acids Screen, Random, Urine; ACRN / Acylcarnitines, Quantitative, Plasma; and AAQP / Amino Acids, Quantitative, Plasma.

Necessary Information

Patient's age, family history, clinical condition (asymptomatic or acute episode), diet, and drug therapy information is requested but not required.

Specimen Required

Patient Preparation: If clinically feasible, discontinue L-carnitine supplementation at least 72 hours before specimen collection.
Supplies: Urine Tubes, 10 mL (T068)
Collection Container/Tube: Clean, plastic urine collection container
Submission Container/Tube: Plastic, 10-mL urine tube
Specimen Volume: 5 mL
Collection Instructions:
1. Collect a random urine specimen.
2. Freeze specimen immediately.

Forms

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

Specimen Minimum Volume

1 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Frozen (preferred)	7 days	
	Refrigerated	24 hours	

Clinical & Interpretive

Clinical Information

The differential diagnosis of an isolated elevation of 3-hydroxyisovaleryl-/2-methyl-3-hydroxy acylcarnitine (C5-OH) in plasma or (newborn screening) blood spots includes the following disorders:
-3-Methylcrotonyl-CoA carboxylase deficiency (common name: 3-methylcrotonylglycinuria), either infantile or maternal
-3-Hydroxy 3-methylglutaryl-CoA lyase deficiency
-Beta-ketothiolase deficiency
-2-Methyl 3-hydroxybutyryl-CoA dehydrogenase deficiency
-3-Methylglutaconic aciduria type I

-Biotinidase deficiency
-Holocarboxylase deficiency

Confirmatory and diagnostic testing are necessary to differentiate these clinical entities. This test can be used to differentiate patients with 3-methylcrotonylglycinuria and with 3-methylglutaconic aciduria as they typically excrete larger amounts of C5-OH in urine compared to patients with the other diagnoses.

The American College of Medical Genetics and Genomics Newborn Screening Work Group published diagnostic algorithms for the follow-up of infants who had positive newborn screening results. For more information, see the Practice Resources: ACT Sheets and Algorithms at www.acmg.net.

Reference Values
<2.93 millimoles/mole creatinine

Interpretation
Preliminary data showed that an elevated excretion in urine and concentration in plasma of 3-hydroxyisovaleryl-/2-methyl-3-hydroxy acylcarnitine can be the only biochemical abnormalities in patients with 3-methylcrotonylglycinuria.

Cautions
The results of urine acylcarnitines are typically not informative when the patient is receiving L-carnitine supplements.

Clinical Reference
1. Wolfe LA, Finegold DN, Vockley J, et al. Potential misdiagnosis of 3-methylcrotonyl-coenzyme A carboxylase deficiency associated with absent or trace urinary 3-methylcrotonylglycine. Pediatrics. 2007;120(5):e1335-1340
2. Miller MJ, Cusmano-Ozog K, Oglesbee D, Young S; ACMG Laboratory Quality Assurance Committee: Laboratory analysis of acylcarnitines, 2020 update: a technical standard of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021;23(2):249-258

Performance

Method Description
Acylcarnitines, including 3-hydroxy isovalerylcarnitine, are determined in urine by flow injection analysis tandem mass spectrometry using acetyl-d3-carnitine, propionyl-d3-carnitine, butyryl-d3-carnitine, octanoyl-d3-carnitine, dodecanoyl-d3-carnitine, and palmitoyl-d3-carnitine as internal standards. The supernatant is evaporated and the residue treated with n-butanolic hydrochloric acid yielding the acylcarnitines for analysis as their n-butyl esters.(Tortorelli S, Hahn SH, Cowan TM, Brewster TG, Rinaldo P, Matern D. The urinary excretion of glutarylcarnitine is an informative tool in the biochemical diagnosis of glutaric acidemia type I. Mol Genet Metab. 2005;84[2]:137-143)

PDF Report
No

Day(s) Performed

Monday, Wednesday, Friday

Report Available
2 to 5 days

Specimen Retention Time
1 month

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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
82017

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
C5OHU	C5-OH Acylcarnitine, QN, U	50091-8

Result ID	Test Result Name	Result LOINC® Value
88830	C5-OH Acylcarnitine, QN, U	50091-8
28125	C5-OH Interpretation	59462-2
34469	Reviewed By	18771-6