MAYO CLINIC LABORATORIES

# Test Definition: ACRNS

Acylcarnitines, Quantitative, Serum

## Overview

### Useful For

Diagnosis of fatty acid oxidation disorders and several organic acidurias using serum specimens

Evaluating treatment during follow-up of patients with fatty acid beta-oxidation disorders and several organic acidurias

### Method Name

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

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Necessary Information

**1. Patient's age is required.**

2. Include family history, clinical condition (asymptomatic or acute episode), diet, and drug therapy information.

### Specimen Required

**Patient Preparation:** Collect specimen just prior to a scheduled meal or feeding.

**Collection Container/Tube:**

**Preferred:** Serum gel

**Acceptable:** Red top

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 0.1 mL

**Collection Instructions:** Centrifuge and aliquot serum into plastic vial.

### Forms

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

### Specimen Minimum Volume

0.04 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | OK |
| Gross lipemia | OK |

| | |
|---|---|
| Gross icterus | OK |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Serum | Frozen (preferred) | 60 days | |
| | Refrigerated | 21 days | |
| | Ambient | 72 hours | |

## Clinical & Interpretive

### Clinical Information

Acylcarnitine analysis enables the diagnosis of many disorders of fatty acid oxidation and several organic acidurias, as relevant enzyme deficiencies cause the accumulation of specific acyl-CoAs.(1) Fatty acid oxidation (FAO) plays a major role in energy production during periods of fasting. When the body's supply of glucose is depleted, fatty acids are mobilized from adipose tissue, taken up by the liver and muscles, and oxidized to acetyl-CoA. In the liver, acetyl-CoA is the building block for the synthesis of ketone bodies, which enter the blood stream and provide an alternative substrate for production of energy in other tissues when the supply of glucose is insufficient to maintain a normal level of energy. The acyl groups are conjugated with carnitine to form acylcarnitines, which can be measured by tandem mass spectrometry. Diagnostic results are usually characterized by a pattern of significantly elevated acylcarnitine species compared to normal and disease controls.

In general, more than 20 inborn errors of metabolism can be identified using this method including FAO disorders and organic acidurias. The major clinical manifestations associated with individual FAO disorders include hypoketotic hypoglycemia, variable degrees of liver disease or failure, skeletal myopathy, dilated/hypertrophic cardiomyopathy, and sudden or unexpected death. Organic acidurias also present as acute life-threatening events early in life with metabolic acidosis, increased anion gap, and neurologic distress. Patients with any of these disorders are at risk of developing fatal metabolic decompensations following the acquisition of even common infections. Once diagnosed, these disorders can be treated by avoidance of fasting, special diets, and cofactor/vitamin supplementation.

Additional confirmatory testing is recommended. The diagnosis of an underlying FAO disorder or organic aciduria allows genetic counseling of the family, including the possible option of future prenatal diagnosis, and testing of at-risk family members of any age.

The following disorders are detectable by acylcarnitine analysis. However, further confirmatory testing is required for most of these conditions because an acylcarnitine profile can be suggestive of more than one condition.

Fatty Acid Oxidation Disorders:
-Carnitine palmitoyltransferase I deficiency
-Medium-chain 3-ketoacyl-CoA thiolase deficiency
-Dienoyl-CoA reductase deficiency
-Short-chain acyl-CoA dehydrogenase deficiency
-Medium/Short-chain 3-hydroxyacyl-CoA dehydrogenase deficiency
-Medium-chain acyl-CoA dehydrogenase) deficiency

-Long-chain 3-hydroxyacyl-CoA dehydrogenase) deficiency and trifunctional protein deficiency
-Very long-chain acyl-CoA dehydrogenase deficiency
-Carnitine palmitoyl transferase type II deficiency
-Carnitine-acylcarnitine translocase deficiency
-Electron transfer flavoprotein (ETF) deficiency, ETF-dehydrogenase deficiency (multiple acyl-CoA dehydrogenase deficiency; glutaric acidemia type II)

Organic Acid Disorders:
-Glutaryl-CoA dehydrogenase deficiency (glutaric acidemia type I)
-Propionic acidemia
-Methylmalonic acidemia
-Isovaleric acidemia
-3-Hydroxy-3-methylglutaryl-CoA carboxylase deficiency
-3-Methylcrotonyl carboxylase deficiency
-Biotinidase deficiency
-Multiple carboxylase deficiency
-Isobutyryl-CoA dehydrogenase deficiency
-2-Methylbutyryl-CoA dehydrogenase deficiency
-Beta-ketothiolase deficiency
-Malonic aciduria
-Ethylmalonic encephalopathy
-Glutamate formiminotransferase deficiency (formiminoglutamic aciduria)

## Reference Values

| | < or =7 days (nmol/mL) | 8 days-7 years (nmol/mL) | > or =8 years (nmol/mL) |
|---|---|---|---|
| Acetylcarnitine, C2 | 2.14-15.89 | 2.00-27.57 | 2.00-17.83 |
| Acrylylcarnitine, C3:1 | <0.04 | <0.05 | <0.07 |
| Propionylcarnitine, C3 | <0.55 | <1.78 | <0.88 |
| Formiminoglutamate, FIGLU | <0.43 | <0.08 | <0.14 |
| Iso-/Butyrylcarnitine, C4 | <0.46 | <1.06 | <0.83 |
| Tiglylcarnitine, C5:1 | <0.05 | <0.09 | <0.11 |
| Isovaleryl-/2-Methylbutyrylcarn C5 | <0.38 | <0.63 | <0.51 |
| 3-OH-iso-/butyrylcarnitine, C4-OH | <0.13 | <0.51 | <0.18 |
| Hexenoylcarnitine, C6:1 | <0.12 | <0.10 | <0.15 |
| Hexanoylcarnitine, C6 | <0.14 | <0.23 | <0.17 |
| 3-OH-isovalerylcarnitine, C5-OH | <0.08 | <0.12 | <0.10 |
| Benzoylcarnitine | <0.13 | <0.07 | <0.10 |
| Heptanoylcarnitine, C7 | <0.05 | <0.05 | <0.06 |
| 3-OH-hexanoylcarnitine, C6-OH | <0.08 | <0.19 | <0.09 |
| Phenylacetylcarnitine | <0.15 | <0.22 | <0.29 |
| Salicylcarnitine | <0.08 | <0.09 | <0.09 |
| Octenoylcarnitine, C8:1 | <0.48 | <0.91 | <0.88 |
| Octanoylcarnitine, C8 | <0.19 | <0.45 | <0.78 |

| | | | |
|---|---|---|---|
| Malonylcarnitine, C3-DC | <0.09 | <0.14 | <0.26 |
| Decadienoylcarnitine, C10:2 | <0.11 | <0.12 | <0.26 |
| Decenoylcarnitine, C10:1 | <0.25 | <0.46 | <0.47 |
| Decanoylcarnitine, C10 | <0.27 | <0.91 | <0.88 |
| Methylmalonyl-/succinylcarn, C4-DC | <0.05 | <0.05 | <0.05 |
| 3-OH-decenoylcarnitine, C10:1-OH | <0.12 | <0.12 | <0.13 |
| Glutarylcarnitine, C5-DC | <0.06 | <0.10 | <0.11 |
| Dodecenoylcarnitine, C12:1 | <0.19 | <0.37 | <0.35 |
| Dodecanoylcarnitine, C12 | <0.18 | <0.35 | <0.26 |
| 3-Methylglutarylcarnitine, C6-DC | <0.28 | <0.21 | <0.43 |
| 3-OH-dodecenoylcarnitine, C12:1-OH | <0.11 | <0.10 | <0.13 |
| 3-OH-dodecanoylcarnitine, C12-OH | <0.06 | <0.09 | <0.08 |
| Tetradecadienoylcarnitine, C14:2 | <0.09 | <0.13 | <0.18 |
| Tetradecenoylcarnitine, C14:1 | <0.16 | <0.35 | <0.24 |
| Tetradecanoylcarnitine, C14 | <0.11 | <0.15 | <0.12 |
| Octanedioylcarnitine, C8-DC | <0.25 | <0.19 | <0.19 |
| 3-OH-tetradecenoylcarnitine C14:1OH | <0.06 | <0.18 | <0.13 |
| 3-OH-tetradecanoylcarnitine, C14-OH | <0.04 | <0.05 | <0.08 |
| Hexadecenoylcarnitine, C16:1 | <0.15 | <0.21 | <0.10 |
| Hexadecanoylcarnitine, C16 | <0.36 | <0.52 | <0.23 |
| 3-OH-hexadecenoylcarnitine,C16:1-OH | <0.78 | <0.36 | <0.06 |
| 3-OH-hexadecanoylcarnitine, C16-OH | <0.10 | <0.07 | <0.06 |
| Octadecadienoylcarnitine, C18:2 | <0.12 | <0.31 | <0.24 |
| Octadecenoylcarnitine, C18:1 | <0.25 | <0.45 | <0.39 |
| Octadecanoylcarnitine, C18 | <0.10 | <0.12 | <0.14 |
| Dodecanedioylcarnitine, C12-DC | <0.10 | <0.04 | <0.04 |
| 3-OH-octadecadienoylcarn, C18:2-OH | <0.04 | <0.06 | <0.06 |
| 3-OH-octadecenoylcarnitine C18:1-OH | <0.03 | <0.04 | <0.06 |
| 3-OH-octadecanoylcarnitine, C18-OH | <0.03 | <0.05 | <0.03 |

## Interpretation

An interpretive report will be provided. The individual quantitative results support the interpretation of the acylcarnitine profile but are not diagnostic by themselves. The interpretation is based on pattern recognition.

Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on an acylcarnitine analysis, independent biochemical (eg, in vitro enzyme assay) or molecular genetic analyses are required.

## Cautions

In a few instances, false-negative results occur in the analysis of acylcarnitine profiles. For some disorders, such as medium-chain acyl-CoA dehydrogenase deficiency, the calculation of ratios between different acylcarnitine species provides a discriminate factor to overcome such problems. Where applicable, the calculation of such ratios will be incorporated in the routine acylcarnitine analysis. Informative profiles may also not be detected in some disorders where the accumulation of diagnostic acylcarnitines is a reflection of the residual activity of the defective enzyme, the

dietary load of precursors, and the anabolic/catabolic and treatment statuses of a patient.

Patients with carnitine deficiency may not exhibit abnormally high acylcarnitine concentrations. If the results are indicative for carnitine deficiency, the interpretation will include a remark that this limits the diagnostic value of the test and repeat analysis may be considered following carnitine supplementation.

Follow-up testing such as in vitro enzyme assays or molecular genetic testing may be recommended following abnormal acylcarnitine results. It is not advisable to intentionally stress the patient's metabolism (eg, fasting test) prior to specimen collection for acylcarnitine analysis.

### Clinical Reference

1. 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
2. Matern D. Acylcarnitines, including in vitro loading tests. In: Blau N, Duran M, Gibson KM, eds. Laboratory Guide to the Methods in Biochemical Genetics. Springer Verlag; 2008:171-206
3. Rinaldo P, Cowan TM, Matern D. Acylcarnitine profile analysis. Genet Med. 2008;10(2):151-156
4. Smith EH, Matern D. Acylcarnitine analysis by tandem mass spectrometry. Curr Protoc Hum Genet. 2010;Chap 17:Unit 17.8.1-20
5. Elizondo G, Matern D, Vockley J, Harding CO, Gillingham MB. Effects of fasting, feeding and exercise on plasma acylcarnitines among subjects with CPT2D, VLCADD and LCHADD/TFPD. Mol Genet Metab. 2020;131(1-2):90-97

## Performance

### Method Description

To 20 mcL of serum, 6 internal standards of known concentration (d3-acetylcarnitine, d3-propionylcarnitine, d7-butyrylcarnitine, d3-octanoylcarnitine, d3-dodecanoylcarnitine, and d3-palmitoyl-carnitine) and acetonitrile for deproteinization are added. Following shaking for 30 minutes and centrifugation, the supernate is dried and then treated with n-butanolic HCl yielding the acylcarnitines, which are analyzed as their n-butylesters by electrospray ionization tandem mass spectrometry. The concentrations of the analytes are established by computerized comparison of these analytes' ion intensities to those of the closest internal standard.(Van Hove JL, Kahler SG, Feezor MD, et al. Acylcarnitines in plasma and blood spots of patients with long-chain 3-hydroxyacylcoenzyme A dehydrogenase deficiency. J Inherit Metab Dis. 2000;23(6):571-582; 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)

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

2 to 5 days

### Specimen Retention Time

1 month

### 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

82017

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| ACRNS | Acylcarnitines, Quantitative, S | 43433-2 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 92134 | Acetylcarnitine, C2 | 30191-1 |
| 92135 | Acrylylcarnitine, C3:1 | 43235-1 |
| 92136 | Propionylcarnitine, C3 | 30551-6 |
| 92137 | Formiminoglutamate, FIGLU | 79628-4 |
| 92138 | Iso-/Butyrylcarnitine, C4 | 35655-0 |
| 92139 | Tiglylcarnitine, C5:1 | 51416-6 |
| 92140 | Isovaleryl-/2-Methylbutyrylcarn C5 | 30531-8 |
| 92141 | 3-OH-iso-/butyrylcarnitine, C4-OH | 39000-5 |
| 92142 | Hexenoylcarnitine, C6:1 | 74540-6 |
| 92143 | Hexanoylcarnitine, C6 | 30358-6 |
| 92144 | 3-OH-isovalerylcarnitine, C5-OH | 39001-3 |
| 92145 | Benzoylcarnitine | 39615-0 |
| 92146 | Heptanoylcarnitine, C7 | 55871-8 |
| 92147 | 3-OH-hexanoylcarnitine, C6-OH | 30236-4 |
| 92148 | Phenylacetylcarnitine | 90237-9 |
| 92149 | Salicylcarnitine | 90238-7 |

| | | |
|---|---|---|
| 92150 | Octenoylcarnitine, C8:1 | 30541-7 |
| 92151 | Octanoylcarnitine, C8 | 30540-9 |
| 92152 | Malonylcarnitine, C3-DC | 55940-1 |
| 92153 | Decadienoylcarnitine, C10:2 | 53471-9 |
| 92154 | Decenoylcarnitine, C10:1 | 30328-9 |
| 92156 | Methylmalonyl-/succinylcarn, C4-DC | 51415-8 |
| 92157 | 3-OH-decenoylcarnitine, C10:1-OH | 82478-9 |
| 92155 | Decanoylcarnitine, C10 | 30327-1 |
| 92158 | Glutarylcarnitine, C5-DC | 30349-5 |
| 92159 | Dodecenoylcarnitine, C12:1 | 30332-1 |
| 92160 | Dodecanoylcarnitine, C12 | 30331-3 |
| 92161 | 3-Methylglutarylcarnitine, C6-DC | 39002-1 |
| 92162 | 3-OH-dodecenoylcarnitine, C12:1-OH | 59195-8 |
| 92163 | 3-OH-dodecanoylcarnitine, C12-OH | 30233-1 |
| 92164 | Tetradecadienoylcarnitine, C14:2 | 30564-9 |
| 92165 | Tetradecenoylcarnitine, C14:1 | 30566-4 |
| 92166 | Tetradecanoylcarnitine, C14 | 30565-6 |
| 92167 | Octanedioylcarnitine, C8-DC | 39014-6 |
| 92168 | 3-OH-tetradecenoylcarnitine C14:1OH | 30190-3 |
| 92169 | 3-OH-tetradecanoylcarnitine, C14-OH | 30238-0 |
| 92170 | Hexadecenoylcarnitine, C16:1 | 30357-8 |
| 92171 | Hexadecanoylcarnitine, C16 | 30356-0 |
| 92172 | 3-OH-hexadecenoylcarnitine,C16:1-OH | 30235-6 |
| 92173 | 3-OH-hexadecanoylcarnitine, C16-OH | 30234-9 |
| 92174 | Octadecadienoylcarnitine, C18:2 | 30534-2 |
| 92175 | Octadecenoylcarnitine, C18:1 | 30542-5 |
| 92176 | Octadecanoylcarnitine, C18 | 30560-7 |
| 92177 | Dodecanedioylcarnitine, C12-DC | 55855-1 |
| 92178 | 3-OH-octadecadienoylcarn, C18:2-OH | 30237-2 |
| 92179 | 3-OH-octadecenoylcarnitine C18:1-OH | 30312-3 |
| 92180 | 3-OH-octadecanoylcarnitine, C18-OH | 35656-8 |
| 92181 | Comment (ACRNS) | 46252-3 |