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## Overview

### Useful For

Postmortem evaluation of individuals at any age who died suddenly or unexpectedly; testing is particularly recommended under the following circumstances (risk factors):

- Family history of sudden infant death syndrome or other sudden unexpected deaths at any age
- Family history of Reye syndrome
- Maternal complications of pregnancy (acute fatty liver pregnancy, HELLP syndrome [hemolysis, elevated liver enzymes, and low platelet count])
- Lethargy, vomiting, fasting in the 48 hours prior to death
- Allegation of child abuse (excluding obvious cases of trauma, physical harm)
- Macroscopic findings at autopsy:
  - Fatty infiltration of the liver
  - Dilated or hypertrophic cardiomyopathy
  - Autopsy evidence of infection that routinely would not represent a life-threatening event

### Genetics Test Information

Acylcarnitine analysis in blood and bile specimens to evaluate cases of sudden or unexpected death. Confirmatory enzymatic and molecular studies of cultured fibroblasts may be recommended.

### Highlights

Analysis of acylcarnitines in blood and bile spots represents the first level of evaluation of a complete postmortem investigation of a sudden or unexpected death of an individual at any age.

Analysis facilitates the diagnosis of over 20 inborn errors of metabolism including fatty acid oxidation disorders and organic acidurias.

Abnormal results are not always sufficient to conclusively establish a diagnosis of a particular disease. When abnormal results are obtained, additional confirmatory testing is recommended.

Detailed reports for abnormal acylcarnitine profiles are provided that include an overview of the results and recommendations for follow-up.

### Testing Algorithm

See [Postmortem Screening Algorithm](#) in Special Instructions.

### Special Instructions

- [Request for Original Newborn Screening Card](#)
- [Postmortem Screening Algorithm](#)

### Method Name

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Electrospray Tandem Mass Spectrometry (MS/MS)

**NY State Available**

Yes

**Specimen****Specimen Type**

Whole blood

**Necessary Information**

Request the original newborn screening card from the state laboratory where the decedent was born. See [Request for Original Newborn Screening Card](#) in Special Instructions.

**Specimen Required**

**Both bile and blood spots are required.**

**Supplies:** Card-Postmortem Screening (Filter Paper) (T525)

**Collection Container/Tube:** Postmortem Screening Card

**Specimen Volume:** Properly completed screening card

**Collection Instructions:**

1. Collect blood in a heparin-containing tube and drop 25 mcL of blood onto the 2 circles labeled Blood.
2. Collect bile by direct puncture of the gallbladder and drop 25 mcL of bile onto the 2 circles labeled Bile.
3. Allow to dry at ambient temperature in a horizontal position for 3 or more hours.
4. Fill out information on page 2 of collection card.
5. Do not expose specimen to heat or direct sunlight.
6. Do not stack wet specimens.
7. Keep specimen dry.

**Forms**

If not ordering electronically, complete, print, and send an [Inborn Errors of Metabolism Test Request](#) (T798) with the specimen.

**Specimen Minimum Volume**

Bile spot: 1

Blood spot: 1

**Reject Due To**

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

## Specimen Stability Information

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

## Clinical and Interpretive

### Clinical Information

Postmortem screening involves acylcarnitine analysis in blood and bile specimens to evaluate cases of sudden or unexpected death. [Acylcarnitine analysis can diagnose disorders of fatty acid oxidation and several organic acidurias, as relevant enzyme deficiencies cause the accumulation of specific acyl-CoAs measured by this assay. 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 are measured by tandem mass spectrometry \(MS/MS\). 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 and 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 and vitamin supplementation.

Analysis of acylcarnitines in blood and bile spots represents the first level of evaluation of a complete postmortem investigation of a sudden or unexpected death of an individual. 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.

Disorders Detectable by Acylcarnitine Analysis\*

#### Fatty Acid Oxidation Disorders:

- Short-chain acyl-CoA dehydrogenase (SCAD) deficiency
- Medium/Short-chain 3-hydroxyacyl-CoA dehydrogenase (M/SCHAD) deficiency
- Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency
- Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency and trifunctional protein deficiency
- Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency

- Carnitine palmitoyl transferase type II (CPT-II) deficiency
- Carnitine-acylcarnitine translocase (CACT) deficiency
- Electron-Transferring Flavoproteins (ETF) deficiency, ETF-dehydrogenase deficiency (multiple acyl-CoA dehydrogenase deficiency: MADD; 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

\*Further confirmatory testing is required for most of these conditions because an acylcarnitine profile can be suggestive of more than 1 condition.

See [Postmortem Screening Algorithm](#) in Special Instructions.

**Reference Values**

Quantitative results are compared to a constantly updated range which corresponds to the 5 to 95 percentile interval of all postmortem cases analyzed in our laboratory.

**Interpretation**

Reports of abnormal acylcarnitine profiles will include an overview of the results and of their significance, a correlation to available clinical information, possible differential diagnoses, recommendations for additional biochemical testing and confirmatory studies (enzyme assay, molecular analysis) as indicated, name and phone number of contacts who may provide these studies at Mayo Clinic or elsewhere, and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Abnormal results are not always sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on an acylcarnitine analysis, independent biochemical (eg, FAO / Fatty Acid Oxidation Probe Assay, Fibroblast Culture) or molecular genetic analyses are required using additional tissue such as skin fibroblasts from the deceased patient. If not available, molecular genetic analysis of a patient's parents may enable the confirmation of a diagnosis.

### Cautions

Both blood and bile specimens must be collected in order to detect and independently confirm the largest possible number of disorders. However, if only 1 specimen type is available, testing is still beneficial.

In cases with a higher level of suspicion due to the recognition of 1 or more risk factors, collection of urine on filter paper and a skin biopsy is also recommended for further testing and enzymatic/molecular studies. Contact the Biochemical Genetic consultant or genetic counselor on call at 800-533-1710 to discuss high-risk cases.

In comparison to living individuals, profiles of postmortem blood specimens generally show a nonspecific increase of short chain species.

Patients with secondary carnitine deficiency may display uninformative acylcarnitine profiles in blood, but not in bile.

Several fatty acid oxidation disorders are not associated with abnormal acylcarnitine profiles (eg, carnitine palmitoyltransferase I (CPT I) deficiency, 3-hydroxy-3-methylglutaryl CoA synthase (HMG-CoA synthase) deficiency) and will not be detected.

### Clinical Reference

1. Rinaldo P, Matern D, Bennet BJ: Fatty acid oxidation disorders. *Ann Rev Physiol* 2002;64:477-502
2. Rashed MS, Ozand PT, Bennett MJ, et al: Inborn errors of metabolism diagnosed in sudden death cases by acylcarnitine analysis of postmortem bile. *Clin Chem* 1995;41:1109-1114
3. Pryce JW, Weber MA, Heales S, et al: Tandem mass spectrometry findings at autopsy for detection of metabolic disease in infant deaths: postmortem changes and confounding factors. *J Clin Pathol* 2011;64:1005-1009. doi: 10.1136/jclinpath-2011-200218

### Performance

#### Method Description

Blood and bile are collected on the same filter paper card; newborn screening filter paper cards are used. Blood drawn into heparin-containing tubes and bile collected by direct puncture of the gallbladder are spotted on a filter paper card. Two circles are labeled and used for blood, 2 circles are labeled and used for bile (each 25 mcL of volume). A 3/16" disk is punched out of the dried blood or 1/16" dried bile spot into an Eppendorf tube. The acylcarnitines are extracted by the addition of methanol and known concentrations of isotopically labeled acylcarnitines as internal standards. The extract is transferred to a Reacti-Vial, dried under a stream of nitrogen, and derivatized by the addition of *n*-butanol hydrochloric acid. The acylcarnitines are measured as their butyl esters by electrospray tandem mass spectrometry. The concentration of the analytes is established by computerized comparison of ion intensities of these analytes to that of the respective internal standards. (Chace DH, DiPerna JC, Mitchell BL, et al: Electrospray tandem mass spectrometry for analysis of acylcarnitines in dried postmortem blood specimens collected at autopsy from infants with unexplained cause of death. *Clin Chem* 2001;47:1166-1182)

#### PDF Report

No

**Day(s) and Time(s) Test Performed**

Thursday

**Analytic Time**

7 days

**Maximum Laboratory Time**

16 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**

83789

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
PMSBB	Postmortem Screening	In Process

Result ID	Test Result Name	Result LOINC Value
22675	Specimen	31208-2
22676	Specimen ID	57723-9
22677	Source	31208-2
22678	Order Date	82785-7
22679	Reason For Referral	42349-1
22680	Method	49549-9
22684	Results	58088-6
81931	Interpretation	59462-2
22681	Amendment	48767-8
22682	Reviewed By	18771-6



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Result ID	Test Result Name	Result LOINC Value
22683	Release Date	82772-5