MAYO CLINIC LABORATORIES

Test Definition: MCADZ

Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency Full Gene Analysis, Varies

Overview

Useful For

Confirmation of diagnosis of medium-chain acyl-CoA dehydrogenase (MCAD) deficiency (as a follow-up to biochemical analyses)

Screening of at-risk carriers of MCAD deficiency when an affected relative has not had molecular testing

Diagnosis of MCAD deficiency in autopsy specimens

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No

Testing Algorithm

For skin biopsy or cultured fibroblast specimens, fibroblast culture testing will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Special Instructions

- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name

Polymerase Chain Reaction (PCR) Amplification/DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

Preferred:
Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Any anticoagulant
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.
Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Cultured fibroblasts
Container/Tube: T-75 or T-25 flask
Specimen Volume: 1 Full T-75 or 2 full T-25 flasks
Specimen Stability Information: Ambient (preferred)/Refrigerated <24 hours
Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type: Skin biopsy
Container/Tube: Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin. Tubes can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin [T115]).
Specimen Volume: 4-mm punch
Specimen Stability Information: Refrigerated (preferred)/Ambient
Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type: Blood spot
Supplies: Card - Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Collection card (Whatman Protein Saver 903 Paper)
Acceptable: Ahlstrom 226 filter paper or blood spot collection card
Specimen Volume: 2 to 5 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient 1 year of age or older is a fingerstick. For infants younger than 1

year, a heel stick should be used. See How to Collect Dried Blood Spot Samples via fingerstick.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry
Specimen Stability Information: Ambient (preferred)/Refrigerated
Additional Information:
1. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
2. For collection instructions, see Blood Spot Collection Instructions
3. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
4. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

Forms
1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Molecular Genetics: Biochemical Disorders Patient Information (T527) in Special Instructions

Specimen Minimum Volume
Blood: 1 mL
Blood Spots: 5 punches, 3-mm diameter

Reject Due To
All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information
Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is an autosomal recessive inherited defect in the mitochondrial oxidation of fatty acids. The mitochondrial beta-oxidation pathway plays a major role in energy production, especially during periods of fasting and physical exertion. MCAD deficiency is prevalent among individuals of northern European origin, affecting 1 in 4,900 to 1 in 17,000 individuals, with a carrier frequency estimated as high as 1 in 40 for some populations.

Phenotypic expression of MCAD deficiency is episodic in nature (ie, asymptomatic between attacks). Symptoms are typically precipitated by any stress (eg, fever, infection, vaccination) and mostly occur during the first 2 years of life, although some cases have been diagnosed in adulthood. Characteristic features of MCAD deficiency include: Reye-like

syndrome (an acquired encephalopathy characterized by recurrent vomiting, agitation, and lethargy), fasting intolerance with vomiting, recurrent episodes of hypoglycemic coma, hypoketotic dicarboxylic aciduria, low plasma and tissue levels of carnitine, hepatic failure with fat infiltration (fatty liver), encephalopathy, and rapidly progressive deterioration leading to death. MCAD deficiency has also been associated with sudden infant death or sudden unexpected death syndrome.

Review of clinical features and biochemical analysis via plasma acylcarnitines (ACRN / Acylcarnitines, Quantitative, Plasma), fatty acid profile (FAO / Fatty Acid Oxidation Probe Assay, Fibroblast Culture), urine organic acids (OAU / Organic Acids Screen, Urine), and urine acylglycines (ACYLG / Acylglycines, Quantitative, Urine) are always recommended as the initial evaluation for MCAD. If previously performed, the results of these biochemical assays should be included with the specimen as they are necessary for accurate interpretation of the MCAD sequence analysis.

The MCAD gene (*ACADM*) maps to 1p31 and has 12 exons, spanning 44 kb of DNA. Most mutations are family-specific with the exception of the recurrent A->G transition at nucleotide 985 (985A->G). Among MCAD-deficient patients, approximately 52% are homozygous for the 985A->G mutation. The majority of the remaining patients are compound heterozygous for the 985A->G mutation and a different mutation.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of medium-chain acyl-CoA dehydrogenase (MCAD) deficiency may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of MCAD. For carrier testing, it is important to first document the presence of an *ACADM* gene mutation in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015 May;17(5):405-424
2. Grosse SD, Khoury MJ, Greene CL, et al: The epidemiology of medium chain acyl-CoA dehydrogenase deficiency: An

update. Genet Med 2006 April:8(4):205-212
2. Ziadeh R, Hoffman EP, Finegold DM, et al: Medium chain acyl-CoA dehydrogenase deficiency in Pennsylvania: neonatal screening shows high incidence and unexpected mutation frequency. Pediatr Res 1995 May;37(5):675-678
3. Roe CR, Coates PM: Mitochondrial fatty acid oxidation. In The Metabolic and Molecular Bases of Inherited Disease. Vol 1. Seventh edition. Edited by CR Scriver, AL Beaudet, WS Sly, D Valle. New York, McGraw-Hill Book Company, 1995, pp 1501-1533

Performance

Method Description
Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the medium-chain acyl-CoA dehydrogenase (MCAD) gene (*ACADM*).(Highsmith WE: Unpublished Mayo information)

PDF Report
No

Day(s) Performed
Varies

Report Available
14 to 20 days

Specimen Retention Time
Whole Blood: 2 weeks (if available); Extracted DNA: 3 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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81479-Unlisted molecular pathology procedure

Fibroblast Culture for Genetic Test
88233-Tissue culture, skin or solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MCADZ	MCAD Deficiency, Full Gene Analysis	95773-8

Result ID	Test Result Name	Result LOINC® Value
53971	Result Summary	50397-9
53972	Result	82939-0
53973	Interpretation	69047-9
53974	Additional Information	48767-8
53975	Specimen	31208-2
53976	Source	31208-2
53977	Released By	18771-6