MAYO CLINIC LABORATORIES

Test Definition: VLCZ

Very Long Chain Acyl-CoA Dehydrogenase Deficiency, Full Gene Analysis, Varies

Overview

Useful For

Confirmation of a diagnosis of very long chain acyl-CoA dehydrogenase (VLCAD) deficiency

Carrier screening in cases where there is a family history of VLCAD deficiency, but an affected individual is not available for testing or disease-causing mutations have not been identified

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)/DNA Sequencing Analysis

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: Lavender top (EDTA) or yellow top (ACD)
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: 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 (T493)
Specimen Volume: 2 to 5 Blood Spots on collection card (Whatman Protein Saver 903 Paper; Ahlstrom 226 filter paper; or Blood Spot Collection Card)
Collection Instructions:
1. An alternative blood collection option for a patient >1 year of age is finger stick.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 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. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

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

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Molecular Genetics: Biochemical Disorders Patient Information (T527)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

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

Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency is an autosomal recessive disorder of mitochondrial fatty acid beta-oxidation. Mitochondrial beta-oxidation plays a major role in energy production and VLCAD catalyzes the first step in the breakdown of fatty acids that are 14 to 20 carbons long.

VLCAD deficiency has a reported incidence of approximately 1 in 30,000 births and has a variable age of onset that is generally classified into 3 categories. Individuals with the early-onset type present with cardiomyopathy, hypotonia, and hepatomegaly in the first months of life; sudden death is also frequent. Individuals with the early-childhood onset type typically present with hypoketotic hypoglycemia and hepatomegaly without cardiomyopathy. Individuals with the late-onset type of VLCAD deficiency generally present after childhood with intermittent rhabdomyolysis and muscle dysfunction that often manifests as muscle cramps and exercise intolerance.

Review of clinical features and biochemical analysis via plasma acylcarnitines, plasma fatty acid profile, urine organic acids, and fibroblast fatty acid oxidation probe studies are recommended as laboratory evaluations for VLCAD deficiency. Plasma and urine biochemical testing are not reliable for identifying all individuals with VLCAD deficiency or confirming carrier status, as biochemical findings may normalize during periods of good metabolic control. It is uncertain whether skin fibroblast analysis can identify carriers of VLCAD deficiency. The diagnosis is confirmed by molecular testing.

Mutations in the *ACADVL* gene are responsible for VLCAD deficiency. Most mutations are family specific with the exception of the *V283A* mutation (also reported in the literature as *V243A*). This mutation is estimated to account for 20% of pathogenic alleles in patients identified by newborn screening. When this test is ordered, results of biochemical assays should be included with the specimen as they are necessary for accurate interpretation of the VLCAD sequence analysis.

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 very long chain acyl-CoA dehydrogenase

(VLCAD) 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 VLCAD deficiency. For carrier testing, it is important to first document the presence of an *ACADVL* 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. Andresen BS, Olpin S, Poorthuis BJ, et al: Clear correlation of genotype with disease phenotype in very-long-chain acyl-CoA dehydrogenase deficiency. Am J Hum Genet 1999;64:479-494
3. Liebig M, Schymik I, Mueller M, et al: Neonatal screening for very long-chain acyl-CoA dehydrogenase deficiency: enzymatic and molecular evaluation of neonates with elevated C14:1-carnitine levels. Pediatrics 2006;118:1065-1069

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 *ACADVL* gene.(Unpublished Mayo method)

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

Mayo Clinic Laboratories - Rochester Main Campus

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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

81406-ACADV (acyl-CoA dehydrogenase, very long chain) (eg, very long chain acyl-coenzyme A dehydrogenase deficiency), full gene sequence

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
VLCZ	VLCAD Deficiency Full Gene Analysis	73735-3

Result ID	Test Result Name	Result LOINC® Value
54041	Result Summary	50397-9
54042	Result	82939-0
54043	Interpretation	69047-9
54044	Additional Information	48767-8
54046	Source	31208-2
54047	Released By	18771-6
54045	Specimen	31208-2