Overview

Useful For

Diagnosis of Smith-Lemli-Opitz syndrome (7-dehydrocholesterol reductase deficiency)

Highlights

Smith-Lemli-Opitz syndrome (SLO) is a multiple congenital anomaly disorder caused by defective cholesterol biosynthesis due to deficiency of the enzyme 7-dehydrocholesterol reductase.

Clinical variability has been noted, even within families, and the severity of SLO ranges from severe to mild.

Elevated plasma concentrations of 7-dehydrocholesterol (7-DHC) and 8-dehydrocholesterol (8-DHC) are highly suggestive of a biochemical diagnosis of SLO.

Method Name

Gas Chromatography-Mass Spectrometry (GC-MS)

NY State Available

Yes

Specimen

Specimen Type

Plasma

Specimen Required

Collection Container/Tube:

Preferred: Green top (sodium or lithium heparin)

Acceptable: Lavender top (EDTA), pearl white top (EDTA/gel tubes), yellow top (ACD A) or yellow top (ACD B)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Collection Instructions: Centrifuge specimen and aliquot plasma. Send plasma frozen.

Forms

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

Specimen Minimum Volume

0.2 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK

Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Frozen (preferred)	90 days	
	Refrigerated	90 days	

Clinical and Interpretive

Clinical Information

Cholesterol plays an essential role in many cellular and developmental processes. In addition to its role as a membrane lipid, it is the precursor to numerous molecules that play important roles in cell growth and differentiation, protein glycosylation, and signaling pathways. The biosynthesis of cholesterol and its subsequent conversion to other essential compounds is complex, involving a number of intermediates and enzymes. Disorders that result from a deficiency of these enzymes lead to an accumulation of specific intermediates and inhibit the formation of important biomolecules. Clinical findings common to cholesterol biosynthesis disorders include congenital skeletal malformations, dysmorphic facial features, psychomotor retardation, and failure to thrive.

Smith-Lemli-Opitz syndrome (SLO) is an autosomal recessive disorder caused by mutations in the *DHCR7* gene leading to a deficiency of the 7-dehydrocholesterol reductase enzyme. It is characterized biochemically by markedly increased plasma concentrations of 7-dehydrocholesterol (7-DHC) and 8-dehydrocholesterol (8-DHC) levels. Clinically, features can include microcephaly, growth retardation, developmental delay, dysmorphic facial features, cleft palate, limb abnormalities (especially 2-3 syndactyly of the toes and postaxial polydactyly), and heart and kidney malformations. However, the clinical spectrum ranges from mild to severe with some mildly affected individuals presenting with only 2 to 3 toe syndactyly and mild cognitive impairment. The reported incidence is between 1 in 10,000 and 1 in 60,000, but it may be more prevalent due to underdiagnosis of mildly affected individuals.

Other disorders of cholesterol biosynthesis, including desmosterolosis (desmosterol reductase deficiency) and sitosterolemia, may present with similar manifestations. These disorders can be detected biochemically by performing a quantitative profile of plasma sterols (STER / Sterols, Plasma).

Reference Values

Negative (reported as positive or negative)

Quantitative results are provided when positive.

Interpretation

Elevated plasma concentrations of 7-dehydrocholesterol (7-DHC) and 8-dehydrocholesterol (8-DHC) are highly suggestive of a biochemical diagnosis of Smith-Lemli-Opitz (SLO).

Mild elevations of these cholesterol precursors can be detected in patients with hypercholesterolemia and patients treated with haloperidol. However, the 7-DHC to cholesterol ratio is only elevated in SLO patients.

Cautions

Cholesterol screening tests are unreliable for diagnosis for Smith-Lemli-Opitz syndrome.

Aripiprazole and trazodone cause false elevations in 7-dehydrocholesterol.

Clinical Reference

1. Haas D, Kelley RI, Hoffmann GF: Defects of cholesterol biosynthesis. In Pediatric Endocrinology and Inborn Errors of Metabolism. Edited by K Sarafoglou. New York, McGraw-Hill Medical, 2009, pp 313-321

2. Nowaczyk MJM: Smith-Lemli-Opitz Syndrome. In GeneReviews. Edited by RA Pagon, MP Adam, HH Ardinger. University of Washington, Seattle; 1993-2015. 1998 Nov 13 (Updated 2013 Jun 20). Available at www.ncbi.nlm.nih.gov/books/NBK1143/

3. Hall P, Michels V, Gavrilov D, et al: Aripiprazole and trazodone cause elevations of 7-dehydrocholesterol in the absence of Smith-Lemli-Opitz Syndrome. Mol Genet Metab 2013 Sep-Oct;110(1-2):176-178

Performance

Method Description

The plasma specimen is hydrolyzed and then extracted followed by evaporation to dryness under nitrogen. The 7-dehydrocholesterol (7-DHC) is derivatized and the derivatized specimens are analyzed using selected ion-monitoring electron impact gas chromatography-mass spectrometry (GC-MS) to qualitatively screen. When 7-DHC is detected in abnormal concentrations (>1 mcg/mL), quantitative results are provided.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Tuesday, Friday; 8 a.m. (not reported on Saturday or Sunday)

Analytic Time

3 days

Maximum Laboratory Time

9 days

Specimen Retention Time

1 month

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

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
SLO	Smith-Lemli-Opitz Scrn, P	33275-9

Result ID	Test Result Name	Result LOINC Value
81595	Smith-Lemli-Opitz Scrn, P	33275-9
29972	Interpretation	59462-2
29974	Reviewed By	18771-6