

Overview

Useful For

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

Genetics Test Information

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 even within families has been noted and 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 plasma gel), yellow top (ACD A/ACD B)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Collection Instructions:

1. Centrifuge and aliquot plasma into plastic vial.
2. 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

0.1 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)	92 days	
	Refrigerated	28 days	
	Ambient	14 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 variants 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 underdiagnoses 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
7-DEHYDROCHOLESTEROL

< or =2.0 mg/L

8-DEHYDROCHOLESTEROL

< or = 0.3 mg/L

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 some antipsychotic or antidepressant medications including haloperidol, aripiprazole, and trazodone. However, the 7-DHC to cholesterol ratio is typically elevated only in SLO patients.

Cautions

On very rare occasions, 7-dehydrocholesterol is not elevated in patients with Smith-Lemli-Opitz syndrome.

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

Some antipsychotic or antidepressant medications such as aripiprazole and trazodone cause false elevations in 7-dehydrocholesterol.

Clinical Reference

1. Donoghue SE, Pitt JJ, Boneh A, White SM: Smith-Lemli-Opitz syndrome: clinical and biochemical correlates. *J Pediatr Endocrinol Metab.* 2018;31(4):451-459
2. Nowaczyk MJM: Smith-Lemli-Opitz syndrome. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews* [Internet]. University of Washington, Seattle; November 13, 1998. Updated January 30, 2020. Accessed July 20, 2020. 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
4. Genaro-Mattos TC, Tallman KA, Allen LB, et al: Dichlorophenyl piperazines, including a recently-approved atypical antipsychotic, are potent inhibitors of DHCR7, the last enzyme in cholesterol biosynthesis. *Toxicol Appl Pharmacol.* 2018 Jun 15;349:21-28. doi: 10.1016/j.taap.2018.04.029

Performance

Method Description

The plasma specimen is hydrolyzed and then extracted followed by evaporation to dryness under nitrogen. The sterols are derivatized and then analyzed using selected ion-monitoring electron impact gas chromatography-mass spectrometry (GC-MS) to quantitate 7-dehydrocholesterol (7-DHC) and 8-dehydrocholesterol (8-DHC). (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	73852-6

Result ID	Test Result Name	Result LOINC Value
29972	Interpretation	59462-2
610625	7-Dehydrocholesterol	33275-9
610626	8-Dehydrocholesterol	34671-8
29974	Reviewed By	18771-6