MAYO CLINIC LABORATORIES

Test Definition: STER

Sterols, P

Overview

Useful For

Investigation of possible desmosterolosis (desmosterol reductase deficiency), cerebrotendinous xanthomatosis, lathosterolosis, sitosterolemia, sterol C4 methyl oxidase deficiency, MEND (male EBP disorder with neurologic defects) syndrome, and X-linked chondrodysplasia punctata 2

Highlights

This is a screening test for disorders of cholesterol biosynthesis including desmosterolosis, lathosterolosis, cerebrotendinous xanthomatosis, sitosterolemia, sterol C4 methyl oxidase deficiency, and *EBP* gene disorders (X-linked dominant chondrodysplasia punctata type 2 and MEND [male EBP disorder with neurologic defects]syndrome).

Multiple analytes including but not limited to 7-dehydrocholesterol, 8-dehydrocholesterol, desmosterol, lathosterol, campesterol, sitosterol, and cholestanol are included in this test.

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 specimen and aliquot plasma into plastic vial.

2. Send plasma frozen.

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Minimum Volume

0.1 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Frozen (preferred)	92 days	
	Refrigerated	28 days	
	Ambient	14 days	

Clinical & 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 an important role 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.

Desmosterolosis (desmosterol reductase deficiency) is a very rare disorder of cholesterol biosynthesis with a clinical phenotype similar to that of Smith-Lemli-Opitz (SLO) syndrome (7-dehydrocholesterol reductase deficiency). It is caused by variants in *DHCR24* (3-beta-hydroxysterol delta-24-reductase). To date, less than 20 cases of desmosterolosis have been described. Its biochemical marker is the marked elevation of desmosterol in plasma, tissue, and cultured cells.

Another very rare disorder of cholesterol biosynthesis is lathosterolosis caused by variants in *SC5DL* (sterol 3-beta-hydroxysteroid-delta-5-desaturase). Less than 20 patients have been described to date, but the phenotype appears to be characterized by dysmorphic features, multiple congenital anomalies including those of limb and kidney, intellectual disability, and liver disease. Biochemical abnormalities include elevated lathosterol and transaminases, hyperbilirubinemia, and absent 7-dehydrocholesterol.

Sitosterolemia is a rare autosomal recessive disorder caused by variants in the ATP-binding cassette (ABC) transporter genes, *ABCG5* and *ABCG8*, which abnormally enhance the absorption of plant sterols and cholesterol from the intestines. Patients often present with hematologic abnormalities and tendon and tuberous xanthomas as well as premature coronary artery disease. A biochemical diagnosis of sitosterolemia is made by documenting elevations of the plant sterols sitosterol and campesterol in plasma or serum.

Cerebrotendinous xanthomatosis (CTX), also known as 27-hydroxylase deficiency, is caused by variants in the *CYP27A1* gene. CTX is an autosomal recessive sterol storage disease resulting in the accumulation of cholestanol and cholesterol in most tissues and markedly increased levels of cholestanol in serum. Additionally the ketosterol bile acid precursors (7-alpha-hydroxy-4-cholesten-3-one [7a-C4] and 7-alpha,12-alpha–dihydroxycholest-4-en-3-one [7a12aC4]) are elevated in multiple tissues throughout the body and can be measured in blood or plasma, see:

-CTXBS / Cerebrotendinous Xanthomatosis, Blood Spot

-CTXWB / Cerebrotendinous Xanthomatosis, Blood

-CTXP / Cerebrotendinous Xanthomatosis, Plasma

Clinical symptoms, which are variable, develop gradually and can include early chronic diarrhea, followed by bilateral cataracts, tuberous and tendon xanthomas, early atherosclerosis, and progressive neurologic impairment such as ataxia, paraparesis, cerebellar ataxia, and dementia. CTX should be suspected in patients with tendon xanthomas and normal or elevated serum cholesterol, and considered in cases of unexplained juvenile cataracts

X-linked chondrodysplasia punctata 2 (CDPX2) and MEND (male EBP disorder with neurologic defects) syndrome are caused by defects in *EBP,* which codes for emopamil binding protein, an important enzyme in the final steps of the sterol biosynthesis pathway. CDPX2 is a typically male-lethal X-linked dominant skeletal dysplasia with accompanying skin, hair, nail, and eye abnormalities (ichthyosis in the newborn, scarring alopecia, cataracts). The phenotype in affected female patients is variable ranging from severe skeletal and internal anomalies leading to fetal demise or stillbirth to milder short stature or even asymptomatic carriers.

MEND syndrome, caused by nonmosaic partial loss of function variants in *EBP,* affects primarily male patients. It is a

neurologic phenotype characterized by moderate-to-severe developmental delay and central nervous system malformations, in particular Dandy-Walker malformation, agenesis of the corpus callosum, and hydrocephalus. Many patients have dysmorphic features that overlap with Smith-Lemli-Opitz syndrome (2-3 toe syndactyly, postaxial polydactyly, and urogenital anomalies). Female patients are rarely affected.

Biochemical abnormalities for CDXP2 and MEND syndrome include elevated 8(9)-cholestenol and 8-dehydrocholesterol.

Sterol C4 methyl oxidase deficiency (SC4MOL) is an autosomal recessive inborn error of cholesterol metabolism characterized by microcephaly, congenital cataracts, and psoriasiform dermatitis. Other features include immune dysregulation, joint pain, short stature, and intellectual disability. Biochemical abnormalities include increased plasma 4,4'-dimethyl and 4alpha-monomethylsterols such as dihydro T-MAS (4,4'-dimethyl-5alpha-cholesta-8(9)-en-3beta-ol), and decreased total, low-density lipoprotein, and high-density lipoprotein cholesterol.

Reference Values

7-DEHYDROCHOLESTEROL

< or =2.0 mg/L

8-DEHYDROCHOLESTEROL

< or =0.3 mg/L

8(9)-CHOLESTENOL

< or =5.0 mg/L

CAMPESTEROL

< or =8.0 mg/L

CHOLESTANOL

< or =6.0 mg/L

DESMOSTEROL

< or =2.5 mg/L

DIHYDRO T-MAS

< or =0.3 mg/L

LATHOSTEROL

< or =6.0 mg/L

SITOSTEROL

< or =15.0 mg/L

SQUALENE

< or =1.0 mg/L

STIGMASTEROL

< or =0.5 mg/L

Interpretation

A quantitative report of the patient's sterol profile and a Biochemical Genetics consultant's interpretation is provided for each specimen.

Cautions

Reference values were derived using fasting specimens from healthy individuals. Sitosterol and campesterol values may be mildly elevated in individuals whose diets include foods with high concentrations of plant sterols, such as some vegetable oils and infant formulas.

Desmosterol may be elevated in individuals on medications containing amiodarone.(1)

Seven-dehydrocholesterol and 8-dehydrocholesterol may be mildly elevated in individuals on certain antidepressant and/or antipsychotic medications such as aripiprazole and trazodone.(2)

Patients with primary dyslipidemias may also have altered cholesterol metabolism and mild elevations of sterols.(3)

Clinical Reference

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3. Lupatelli G, De Vuono S, Mannarino E: Patterns of cholesterol metabolism: Pathophysiological and therapeutic implications for dyslipidemias and the metabolic syndrome. Nutr Metab Cardiovasc Dis. 2011 Sep;21(9):620-627. doi: 10.1016/j.numecd.2011.04.010

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10. Parraga I, Lopez-Torres J, Andres F, et al: Effect of plant sterols on the lipid profile of patients with hypercholesterolaemia. Randomised, experimental study. BMC Complement Altern Med. 2011;11:73. doi: 10.1186/1472-6882-11-73

Performance

Method Description

The plasma specimen is hydrolyzed and then extracted, followed by evaporation to dryness under nitrogen. The sterols are derivatized and analyzed using selected ion-monitoring electron impact gas chromatography-mass spectrometry (GC-MS) to quantitate 7-dehydrocholesterol, 8-dehydrocholesterol, squalene, 8(9)-cholestenol, cholestanol, desmosterol, lathosterol, DiHydro T-MAS (testis meiosis activating sterol), campesterol, stigmasterol, and sitosterol.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

1 month

Performing Laboratory Location

Rochester

Fees & Codes

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

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
STER	Sterols, P	75858-1

Result ID	Reporting Name	LOINC®
50499	Desmosterol	75739-3
50500	Lathosterol	75740-1
50501	Campesterol	75738-5

50502	Sitosterol	75741-9
29944	Reviewed By	18771-6
29942	Interpretation	59462-2
113381	Cholestanol	2082-6
610622	7-Dehydrocholesterol	33275-9
610623	8-Dehydrocholesterol	34671-8
610620	8(9)-Cholestenol	In Process
610621	DiHydro T-MAS	In Process
610618	Squalene	In Process
610619	Stigmasterol	In Process