

Overview

Useful For

As a component to the initial evaluation of a patient presenting with hepatosplenomegaly

Highlights

This is a screening test for a select number of lysosomal and lipid storage disorders, including cerebrotendinous xanthomatosis (CTX), Gaucher disease, and Niemann-Pick diseases types A, B, and C.

The above conditions may all have hepatosplenomegaly as a presenting sign, making this test a helpful component of a patient's initial evaluation.

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Plasma

Advisory Information

This test should not be used for monitoring of patients with confirmed diagnoses. If a physician is requesting testing for monitoring purposes, see:

CTXP / Cerebrotendinous Xanthomatosis, Plasma

GPSYP / Glucopsychosine, Plasma

OXNP / Oxysterols, Plasma

Specimen Required

Collection Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Sodium heparin, lithium heparin, ACD B

Submission Container/Tube: Plastic vial

Specimen Volume: 0.3 mL

Forms

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

Specimen Minimum Volume

0.25 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Frozen	65 days	

Clinical and Interpretive
Clinical Information

Hepatosplenomegaly is a presenting or accompanying feature for many different inborn errors of metabolism. It typically is a consequence of chronic hepatic dysfunction or abnormal storage of lipids, sugars, or other improperly metabolized analytes due to a particular enzymatic deficiency. The diagnosis can occasionally be narrowed down by consideration of clinical symptoms; however, clinical diagnosis can be difficult due to similarity of clinical features across disorders as well as phenotypic variability. Therefore, screening tests can play an important role in the workup of a patient with hepatosplenomegaly and a suspected lysosomal or lipid storage disorder.

The conditions detected in this assay are Cerebrotendinous Xanthomatosis, Gaucher disease, and Niemann-Pick disease types A, B, and C.

Conditions Identifiable By Method

Disorder	Onset	Analyte Detected	Gene	Incidence
Cerebrotendinous Xanthomatosis (CTX)	Infancy-adulthood	7-alpha-hydroxy-4-cholesten-3-one (7a-C4)	CYP27A1	1 in 50,000 As high as 1 in 400 in Druze population.
		7-alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4)		
Phenotype: early onset diarrhea, cataracts, tendon/cerebral xanthomas, osteoporosis, neuropsychological manifestations, liver disease/hepatosplenomegaly.				

Gaucher Disease	Type I: childhood/adult	glucopsychosine (GPSY)	GBA	Type I: 1 in 30,000 to 1 in 100,000
	Types II/III: neonatal- early childhood			Types II/III: 1 in 100,000
<p>Phenotype: all types exhibit hepatosplenomegaly and hematological abnormalities.</p> <p>Type I: organomegaly, thrombocytopenia, and bone pain. Absence of neurologic symptoms.</p> <p>Types II/III: primary neurologic disease, developmental delay/regression, hepatosplenomegaly, lung disease. Patients with Type II typically die by age 2 to 4. Patients with Type 3 may have a less progressive phenotype and may survive into adulthood.</p>				
Niemann-Pick Type A/B	NPA: neonatal	lyso-sphingomyelin (LSM)	SMPD1	Combined incidence 1 in 250,000
	NPB: birth-adulthood			
<p>Phenotype:</p> <p>NPA: feeding difficulties, jaundice, hepatosplenomegaly, neurologic deterioration, lung disease, hearing and vision impairment, cherry red macula, death usually by age 3.</p> <p>NPB: mainly limited to visceral symptoms; hepatosplenomegaly, stable liver dysfunction, pulmonary compromise, osteopenia.</p>				
Niemann-Pick Type C	Variable (Perinatal-Adulthood)	cholestane-3 beta, 5-alpha, 6-beta-triol (COT)	NPC1 or NPC2	1 in 120,000 to 1 in 150,000
		lyso-sphingomyelin 509 (LSM 509)		
<p>Phenotype: Variable clinical presentation. Ataxia, vertical supranuclear gaze palsy, dystonia, progressive speech deterioration, seizures, +/- hepatosplenomegaly.</p>				

Patients with testing indicative of one of the above disorders should have follow-up enzymatic or molecular testing for confirmation of diagnosis.

Reference Values

CHOLESTANE-3-BETA, 5-ALPHA, 6-BETA-TRIOL

Cutoff: < or =0.070 nmol/mL

7-KETOCHOLESTEROL

Cutoff: < or =0.100 nmol/mL

LYSO-SPHINGOMYELIN

Cutoff: < or =0.100 nmol/mL

GLUCOPSYCHOSINE

Cutoff: < or =0.003 nmol/mL

7-ALPHA-HYDROXY-4-CHOLESTEN-3-ONE (7a-C4)

Cutoff: < or =0.300 nmol/mL

7-ALPHA,12-ALPHA-DIHYDROXYCHOLEST-4-en-3-ONE (7a12aC4)

Cutoff: < or =0.100 nmol/mL

Interpretation

An elevation of 7-alpha-hydroxy-4-cholesten-3-one (7a-C4) and 7-alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4) is strongly suggestive of cerebrotendinous xanthomatosis (CTX).

An elevation of glucopsychosine (GPSY) is indicative of Gaucher disease.

An elevation of lyso-sphingomyelin (LSM) and lyso-sphingomyelin 509 (LSM 509) is highly suggestive of Niemann-Pick type A or B (NPA or NPB) disease.

An elevation of cholestane-3-beta, 5-alpha, 6-beta-triol (COT) lyso-sphingomyelin 509 (LSM 509) is highly suggestive of Niemann-Pick disease type C (NPC).

Cautions

This test is not suitable for the identification of carriers.

Patients with Wolman disease or cholestatic biliary atresia may have a profile similar to Niemann-Pick disease type C (NPC).

Patients with bile acid malabsorption or ileal resection may have elevations of 7-alpha-hydroxy-4-cholesten-3-one (7aC4).

This test does not identify all causes of hepatosplenomegaly.

A positive test result is strongly suggestive of a diagnosis but needs follow-up by stand-alone biochemical or molecular assay.

This test should not be used as a monitoring tool for patients with confirmed diagnoses.

Clinical Reference

1. DeBarber AE, Luo J, Star-Weinstock M, et al: A blood test for cerebrotendinous xanthomatosis with potential for disease detection in newborns. *J. Lipid Res* 2014;55:146-154
2. Federico A, Dotti MT, Gallus GN: Cerebrotendinous Xanthomatosis. In *GeneReviews*. Edited by RA Pagon, MP Adam, HH Ardinger, et al. University of Washington, Seattle. 1993-2017. 2003 Jul 16. Available at www.ncbi.nlm.nih.gov/books/NBK1409/
3. Grabowski GA, Petsko GA, Kolodny EH. et al: Gaucher Disease. In *The Online Metabolic and Molecular Bases of Inherited Disease*. Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York, McGraw-Hill, 2014. Accessed August 11, 2017. Available at <http://ommbid.mhmedical.com/content.aspx?bookid=971§ionid=62643884>
4. Murugeasan V, Chuan WL, Liu J, et al: Glucosylsphingosine is a key biomarker of Gaucher disease. *Am J Hematol* 2016; 91(11):1082-1089
5. Patterson M: Niemann-Pick disease type C. In *GeneReviews*. Edited by RA Pagon, MP Adam, HH Ardinger, et al. Retrieved April 7, 2017. Available at www.ncbi.nlm.nih.gov/books/NBK1296/

Performance**Method Description**

An internal standard is added to an aliquot of plasma, which is then subjected to protein precipitation. Following centrifugation, the supernatant is subjected to liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. The MS/MS is operated in the multiple reaction monitoring (MRM) positive mode to follow the precursor to product species transitions for each analyte and internal standard. The ratio of the extracted peak areas to internal standard is determined by LC-MS/MS is used to calculate the concentration of in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Tuesday, Thursday; 8 a.m.

Analytic Time

2 days (not reported Saturday or Sunday)

Maximum Laboratory Time

8 days

Specimen Retention Time

2 months

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
HSMP	Hepatosplenomegaly Panel, P	92743-4

Result ID	Test Result Name	Result LOINC Value
601542	Interpretation (HSMP)	59462-2
601536	Cholestane-3beta,5alpha,6beta-triol	92755-8
601537	7-Ketocholesterol	92764-0
601538	Lyso-sphingomyelin	92747-5
601539	Glucopsychosine	92750-9
601540	7a-hydroxy-4-cholesten-3-one	92761-6
601541	7a,12a-dihydroxycholest-4-en-3-one	92758-2
601543	Reviewed By	18771-6