Test Definition: HSMWB

Hepatosplenomegaly Panel, Blood

Overview

Useful For

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

This test is **not useful for** the identification of carriers.

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

Highlights

This is a screening test for a select number of lysosomal and lipid storage disorders, including cerebrotendinous xanthomatosis, Gaucher disease, and Niemann-Pick disease types A, B (also known as acid sphingomyelinase deficiency), 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

Whole blood

Ordering Guidance

This test **should not be used** for monitoring patients with confirmed diagnoses. If the testing requested is for monitoring purposes, see:
-CTXWB / Cerebrotendinous Xanthomatosis, Blood
-GPSYW / Glucopsychosine, Blood
-OXYWB / Oxysterols, Blood

This test's clinical sensitivity and specificity for the identification of Niemann-Pick type C (NPC) is 75% and 89%, respectively. If NPC is strongly suspected, the recommended test is HSMP / Hepatosplenomegaly Panel, Plasma.

Specimen Required

Collection Container/Tube:
Preferred: Lavender top (EDTA)

Acceptable: Green top (sodium heparin, lithium heparin), yellow top (ACD B)
Specimen Volume: 1 mL
Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot.**

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics 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
Whole blood	Refrigerated (preferred)	72 hours	
	Ambient	48 hours	

Clinical & 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 presenting with hepatosplenomegaly who may have a lysosomal or lipid storage disorder.

The conditions detected in this assay are cerebrotendinous xanthomatosis, Gaucher disease, and Niemann-Pick (NP) disease types A, B (also known as acid sphingomyelinase deficiency), and, with a lower sensitivity and specificity, NPC.

Patients with abnormal results should have follow-up enzymatic or molecular testing for confirmation of diagnosis.

Table. Conditions Identifiable by Method

Disorder	Onset	Analyte detected	Gene	Incidence
Cerebrotendinous xanthomatosis (CTX)	Infancy - adulthood	7-Alpha-hydroxy-4-cholesten-3-one (7aC4) 7-Alpha,12-aplha-dihydroxycholest-4-en-3-one	*CYP27A1*	1 in 50,000 As high as 1 in 400 in Druze population.

		(12aC4)		
	Phenotype: Early onset diarrhea, cataracts, tendon/cerebral xanthomas, osteoporosis, neuropsychological manifestations, liver disease/hepatosplenomegaly.			
Gaucher disease	Type I: childhood/adult Types II/III: neonatal-early childhood	Glucopsychosine (GPSY)	*GBA*	Type I: 1 in 30,000 to 1 in 100,000 Types II/III: 1 in 100,000
	Phenotype: All types exhibit hepatosplenomegaly and hematological abnormalities. Type I: Organomegaly, thrombocytopenia, and bone pain. Absence of neurologic symptoms. Types II/III: Primary neurologic disease, developmental delay/regression, hepatosplenomegaly, lung disease. Patients with type II typically die by 2 to 4 years of age. Patients with type III may have a less progressive phenotype and may survive into adulthood.			
Niemann-Pick type A/B (NPA, NPB)	NPA: neonatal NPB: birth-adulthood	Lyso-sphingomyelin (LSM) LSM 509	*SMPD1*	Combined incidence 1 in 250,000
	Phenotype: NPA: Feeding difficulties, jaundice, hepatosplenomegaly, neurologic deterioration, lung disease, hearing and vision impairment, cherry red macula, death usually by 3 years of age. NPB: Mainly limited to visceral symptoms; hepatosplenomegaly, stable liver dysfunction, pulmonary compromise, osteopenia.			
Niemann-Pick type C (NPC)	Variable (perinatal-adulthood)	Cholestane-3 beta, 5 alpha, 6 beta-triol (COT) LSM 509	*NPC1* or *NPC2*	1 in 120,000 to 1 in 150,000
	Phenotype: Variable clinical presentation; ataxia, vertical supranuclear gaze palsy, dystonia, progressive speech deterioration, seizures, +/- hepatosplenomegaly.			

Reference Values

Cholestane-3 beta, 5 alpha, 6 beta-triol
Cutoff: < or =0.800 nmol/mL

Lyso-sphingomyelin
Cutoff: < or =0.100 nmol/mL

Glucopsychosine
Cutoff: < or =0.040 nmol/mL

7-Alpha-hydroxy-4-cholesten-3-one (7aC4)
Cutoff: < or =0.750 nmol/mL

7-Alpha,12-aplha-dihydroxycholest-4-en-3-one (12aC4)

Cutoff: < or =0.250 nmol/mL

Interpretation

An elevation of 7-alpha-hydroxy-4-cholesten-3-one (7aC4) and 7-alpha,12-alpha-dihydroxycholest-4-en-3-one (12aC4) is strongly suggestive of cerebrotendinous xanthomatosis.

An elevation particulary of lyso-sphingomyelin (LSM) 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 is highly suggestive of Niemann-Pick disease type C.

An elevation of glucopsychosine is indicative of Gaucher disease.

Cautions

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

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.

Clinical Reference

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2. Federico A, Dotti MT, Gallus GN: Cerebrotendinous xanthomatosis. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2003. Updated March 17, 2022. Accessed November 5, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1409/
3. Grabowski GA, Petsko GA, Kolodny EH: Gaucher disease. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed November 5, 2024. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546056&bookid=2709
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. Wasserstein MP, Schuchman EH. Acid sphingomyelinase deficiency. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2006. Updated April 27, 2023. Accessed November 5, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1370/
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7. Patterson M: Niemann-Pick disease type C. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2000. Updated December 10, 2020. Accessed November 5, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1296/
8. Geberhiwot T, Moro A, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet J Rare Dis. 2018;13(1):50. Published 2018 Apr 6. doi:10.1186/s13023-018-0785-7

Performance

Method Description
Whole blood is spotted on filter paper and dried overnight. A 3-mm dried blood spot is extracted with internal standard. The extract is subjected to liquid chromatography tandem mass spectrometry (LC-MS/MS) analysis. The MS/MS is operated in the multiple reaction monitoring 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 determined by the LC-MS/MS is used to calculate the concentration of in the sample.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Tuesday, Thursday

Report Available
3 to 7 days

Specimen Retention Time
Whole blood: 7 days; Dried blood spot: Normal results: 2 months; Abnormal result: Indefinitely

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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
82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HSMWB	Hepatosplenomegaly Panel, B	92744-2

Test Definition: HSMWB

Hepatosplenomegaly Panel, Blood

Result ID	Test Result Name	Result LOINC® Value
601534	Interpretation (HSMWB)	59462-2
601528	Cholestane-3beta,5alpha,6beta-triol	92756-6
601529	Lyso-sphingomyelin	92748-3
601530	Glucopsychosine	92751-7
601531	7a-hydroxy-4-cholesten-3-one	92762-4
601532	7a,12a-dihydroxycholest-4-en-3-one	92759-0
601535	Reviewed By	18771-6