Test Definition: HSMBS

Hepatosplenomegaly Panel, Blood Spot

Overview

Useful For

As a component of the initial evaluation of a patient presenting with hepatosplenomegaly, using dried blood spot specimens

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

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

Special Instructions

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions

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 of patients with confirmed diagnoses. If a physician is requesting testing for monitoring purposes, see:
-CTXBS / Cerebrotendinous Xanthomatosis, Blood Spot
-GPSY / Glucopsychosine, Blood Spot
-OXYBS / Oxysterols, Blood Spot

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

Supplies:

-Card-Blood Spot Collection (Filter Paper) (T493)

-Card-Postmortem Screening (Filter Paper) (T525)

Container/Tube:

Preferred: Blood Spot Collection card (Filter Paper)

Acceptable: Whatman Protein Saver 903 filter paper, PerkinElmer 226 filter paper, Munktell filter paper, Postmortem Screening Card, or collected with EDTA, sodium heparin, lithium heparin, or ACD B-containing devices

Specimen Volume: 2 Blood spots

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect Dried Blood Spot Samples.
2. Let blood completely dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. At least 1 spot should be complete (ie, unpunched).
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. Keep specimen dry

Additional Information:

1. For collection instructions, see Blood Spot Collection Instructions.
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777).
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800).

Forms

1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

1 Blood spot

Reject Due To

Shows serum rings Insufficient specimen Layering Multiple applications	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	10 days	FILTER PAPER
	Ambient	10 days	FILTER PAPER
	Frozen	59 days	FILTER PAPER

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 (7a-C4) 7-Alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4)	*CYP27A1*	1 in 50,000 As high as 1 in 400 in Druze population
	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	Lyso-sphingomyelin (LSM) LSM 509	*SMPD1*	Combined incidence 1 in 250,000

	NPB: birth-adulthood			
	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 (7a-C4)
Cutoff: < or =0.750 nmol/mL

7-Alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4)
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 particularly 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

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(1):146-154
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, Phil D, 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/.
6. Wasserstein M, Dionisi-Vici C, Giugliani R, et al. Recommendations for clinical monitoring of patients with acid sphingomyelinase deficiency (ASMD). Mol Genet Metab. 2019;126(2):98-105
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. International Niemann-Pick Disease Registry (INPDR): Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet J Rare Dis. 2018;13(1):50. doi:10.1186/s13023-018-0785-7

Performance

Method Description

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
Normal result: 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
HSMBS	Hepatosplenomegaly Panel, BS	92745-9

Result ID	Test Result Name	Result LOINC® Value
601526	Interpretation (HSMBS)	59462-2
601520	Cholestane-3beta,5alpha,6beta-triol	92757-4
601521	Lyso-sphingomyelin	92749-1
601522	Glucopsychosine	92752-5
601523	7a-hydroxy-4-cholesten-3-one	92763-2
601524	7a,12a-dihydroxycholest-4-en-3-one	92760-8
601527	Reviewed By	18771-6