Test Definition: OXYBS

Oxysterols, Blood Spot

Overview

Useful For

Investigating a possible diagnosis of Niemann-Pick disease types A, B, or C using blood spot specimens

Monitoring of individuals with Niemann-Pick disease type C

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

Testing Algorithm

If the patient has abnormal newborn screening results for Niemann- Pick disease, refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1)

For more information see Newborn Screen Follow-up for Acid Sphingomyelinase Deficiency

Special Instructions

- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions
- Newborn Screen Follow-up for Acid Sphingomyelinase Deficiency

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

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 OXNP / Oxysterols, Plasma.

This test is also available as a part of a panel; see HSMBS / Hepatosplenomegaly Panel, Blood Spot. If this test (OXYBS) is ordered with either GPSY / Glucopsychosine, Blood Spot or CTXBS / Cerebrotendinous Xanthomatosis, Blood Spot, the individual tests will be canceled and HSMBS ordered.

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. Let blood dry completely on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
2. At least 1 spot should be complete, (ie, unpunched).
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. 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

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

Niemann-Pick disease types A, B, and C (NPA, NPB, and NPC, respectively) are a group of autosomal recessive lysosomal storage disorders affecting metabolism of specific lipids within cells.

Niemann-Pick disease types A and B, also known as acid sphingomyelinase deficiency, result in extensive storage of sphingomyelin and cholesterol in the liver, spleen, lungs, and may also affect the brain. NPA disease is more severe than NPB, and it is characterized by early onset with feeding problems, dystrophy, persistent jaundice, development of hepatosplenomegaly, neurological deterioration, deafness, and blindness leading to death by 3 years of age. NPB disease is limited to visceral symptoms, such as hepatosplenomegaly, with survival into adulthood. Some patients have been described with intermediary clinical phenotypes. Large, lipid-laden foam cells are characteristic of the disease. Approximately 50% of patient with this condition have cherry-red spots in the macula.

Treatment is available in the form of enzyme replacement therapy, which helps to reduce the accumulation of sphingomyelin; however, it is not effective in treating the central nervous system.

The combined prevalence of NPA and NPB is estimated to be 1 in 250,000 individuals. NPA and NPB are inherited in an autosomal recessive manner and are caused by biallelic disease-causing variants in the *SMPD1* gene. Although there is a higher frequency of type A among the Ashkenazi Jewish population, both types are panethnic. Individuals with NPA and NPB typically have elevations of lyso-sphingomyelin (LSM) and LSM 509 combined with potential elevations in cholestane-3 beta, 5 alpha, 6 beta-triol (COT) or 7-ketocholesterol (7-KC). Molecular genetic testing for NPA and NPB disease is also available (see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify gene list ID: IEMCP-W6S9XD).

Niemann-Pick disease type C is caused by a defect in cellular cholesterol trafficking, which results in the progressive accumulation of unesterified cholesterol in late endosomes/lysosomes. NPC is considered a lipid storage disorder with variable age of onset, from the neonatal period to adulthood, and highly variable clinical presentation. Most individuals are diagnosed during childhood with symptoms that include ataxia, vertical supranuclear gaze palsy, dystonia, progressive speech deterioration, and seizures. Infants may present with or without hepatosplenomegaly and respiratory failure. Those without liver and pulmonary disease may present with hypotonia and developmental delay. Adult-onset NPC is associated with a slower progression and is characterized by psychiatric illness, ataxia, dystonia, and speech difficulties.

New treatments are available for patients with NPC that help improve both the neurological and functional symptoms.

The incidence of NPC is approximately 1 in 120,000 to 150,000 live births. NPC is an autosomal recessive condition and is caused by biallelic disease-causing variants in either the *NPC1* or *NPC2* genes. Most individuals with NPC exhibit elevated levels of oxysterol COT in dried blood spots, however, testing in plasma (OXNP / Oxysterols, Plasma) is more sensitive, particularly in patients with an atypical presentation. Elevations may also be seen in LSM 509 and 7-KC. The diagnosis of NPC can be confirmed by demonstration of impaired cholesterol esterification and positive filipin staining in cultured fibroblasts or by molecular genetic analysis of the *NPC1* and *NPC2* genes (see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify gene list ID: IEMCP-H683JG).

Reference Values

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

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

Interpretation

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

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

Cautions

Nonspecific neonatal cholestasis may result in elevations of cholestane-3-beta, 5-alpha, 6-beta-triol and lyso-sphingomyelin 509.

A normal result in dried blood spots does not rule out Niemann-Pick type C.

Clinical Reference

1. Newborn Screening ACT Sheet [Decreased acid sphingomyelinase] Acid Sphingomyelinase Deficiency (ASMD). American College of Medical Genetics and Genomics; 2022. Revised May 2022. Accessed December 2, 2024. Available at www.acmg.net/PDFLibrary/Niemann-Pick.pdf
2. 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 December 2, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1370/
3.. 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 December 2, 2024.. Available at www.ncbi.nlm.nih.gov/books/NBK1296/
4.Schuchman EH. The pathogenesis and treatment of acid sphingomyelinase-deficient Niemann-Pick disease. Int J Clin Pharmacol Ther. 2009;47(Suppl 1):S48-S57. doi:10.5414/cpp47048.
5. Hollack CEM, de Sonnaville ESV, Cassiman D et al. Acid sphingomyelinase (Asm) deficiency patients in The Netherlands and Belgium: disease spectrum and natural course in attenuated patients. Mol Genet Metab. 2012;107(3):526-533
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. 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
8. Bremova-Ertl T, Claassen J, Foltan T, et al. Efficacy and safety of N-acetyl-L-leucine in Niemann-Pick disease type C. J Neurol. 2022;269(3):1651-1662. doi:10.1007/s00415-021-10717-0
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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

Report Available
3 to 9 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
OXYBS	Oxysterols, BS	92741-8

Result ID	Test Result Name	Result LOINC® Value
36760	Cholestane-3beta,5alpha,6beta-triol	92757-4
36761	Lyso-sphingomyelin	92749-1
36762	Interpretation (OXYBS)	59462-2
36763	Reviewed By	18771-6