
Overview

Useful For

Investigation of possible diagnosis of Niemann-Pick disease types A, B, or C in blood spot specimens

Monitoring of individuals with Niemann-Pick disease type C

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

Testing Algorithm

See [Newborn Screen Follow-up for Niemann Pick Type A and B](#)

For more information, see [Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase](#)

Special Instructions

- [Blood Spot Collection Card-Spanish Instructions](#)
- [Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase](#)
- [Newborn Screen Follow-up for Niemann Pick Type A and B](#)
- [Blood Spot Collection Card-Chinese Instructions](#)
- [Blood Spot Collection Instructions](#)

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 available separately as well as a part of HSMBS / Hepatosplenomegaly Panel, Blood Spot. If this test 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 (Filter Paper)

Acceptable: Whatman Protein Saver 903 filter paper, PerkinElmer 226 (formerly Ahlstrom 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	Reject
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Specimen Stability Information

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

NPA and NPB are caused by a deficiency of sphingomyelinase that results in extensive storage of sphingomyelin and cholesterol in the liver, spleen, lungs, and, to a lesser degree, brain. NPA disease is more severe than NPB and is characterized by early onset with feeding problems, dystrophy, persistent jaundice, development of hepatosplenomegaly, neurological deterioration, deafness, and blindness leading to death by age 3 years of age. NPB disease is limited to visceral symptoms with survival into adulthood. Some patients have been described with intermediary phenotypes. Characteristic of the disease are large lipid-laden foam cells. Approximately 50% of cases have cherry-red spots in the macula. Sphingomyelinase is encoded by the *SMPD1* gene.

The combined prevalence of NPA and NPB is estimated to be 1 in 250,000. NPA and NPB are inherited in an autosomal recessive manner and are caused by 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 lyso-sphingomyelin 509 (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).

[NPC is caused by a defect in cellular cholesterol trafficking that results in the progressive accumulation of unesterified cholesterol in late endosomes/lysosomes.\(1\) NPC is considered a lipid storage disorder with variable age of onset \(range: perinatal period to adulthood\), 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.](#)

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 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 lyso-sphingomyelin 509 (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 (NIEM / Niemann-Pick Type C Detection, 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-TRIOI

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.

An elevation of lyso-sphingomyelin 509 is suggestive of NPA, NPB or NPC disease.

Cautions

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

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

Clinical Reference

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2. OMIM: 257200 Niemann-Pick Disease Type A. Updated October 19, 2016. Accessed February 3, 2021. Available at www.omim.org/entry/257200?search=257200&highlight=257200
3. OMIM: 607616 Niemann-Pick Disease Type B. Updated April 4, 2019. Accessed February 3, 2021. Available at www.omim.org/entry/607616?search=607616&highlight=607616
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5. Patterson MC, Vanier MT, Suzuki K, et al: Niemann-Pick disease type C: a lipid trafficking disorder. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed November 2, 2020. Available at ommbid.mhmedical.com/content.aspx?sectionid=225545907&bookid=2709
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7. Patterson M: Niemann-Pick disease type C. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2000. Updated December 10, 2020. Accessed February 3, 2021. Available at www.ncbi.nlm.nih.gov/books/NBK1296/
8. Schuchman EH: The pathogenesis and treatment of acid sphingomyelinase-deficient Niemann-Pick disease. *Int J Clin Pharmacol Ther.* 2009;47(Suppl 1):S48-S57
9. 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 Nov;107(3):526-533
10. 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 Apr 6;13(1):50

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 is determined by 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

2 to 9 days

Specimen Retention Time

Normal result: 2 months; Abnormal result: Indefinitely

Performing Laboratory Location

Rochester

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 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 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