MAYO CLINIC LABORATORIES

Test Definition: OXNP

Oxysterols, Plasma

Overview

Useful For

Investigation of possible diagnoses of Niemann-Pick disease types A, B, or C in plasma specimens

Monitoring of individuals with Niemann-Pick type C disease

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

Testing Algorithm

The following are available:

-Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase

-Newborn Screen Follow-up for Niemann Pick Type A and B

Special Instructions

- Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase
- Newborn Screen Follow-up for Niemann Pick Type A and B

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Plasma

Ordering Guidance

This test is available separately as well as a part of HSMP / Hepatosplenomegaly Panel, Plasma. If this test is ordered with either GPSYP / Glucopsychosine, Plasma or CTXP / Cerebrotendinous Xanthomatosis, Plasma, the individual tests will be canceled and HSMP ordered.

Specimen Required

Collection Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Green top (sodium heparin or lithium heparin), yellow top (ACD B)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.3 mL

Collection Instructions:

1. Centrifuge at 4 degrees C.
2. Aliquot plasma into plastic vial, taking care not to disturb the buffy coat layer.
3. Send frozen.

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
Plasma	Frozen (preferred)	65 days	

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. 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 or 7-ketocholesterol (7-KC). Molecular genetic testing for NPA and NPB disease is also available (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. Individuals with NPC exhibit elevated levels of oxysterol cholestane-3 beta,5 alpha,6 beta-triol (COT); lyso-sphingomyelin 509 (LSM 509) and 7-ketocholesterol (7-KC) may also be elevated. 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). For molecular confirmation, genetic testing for NPC disease can be performed (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 =0.070 nmol/mL

7-KETOCHOLESTEROL
Cutoff: < or =0.100 nmol/mL

LYSO SPHINGOMYELIN
Cutoff :< or = 0.100 nmol/mL

Interpretation

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

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

An elevation of lyso-sphingomyelin 509 (LSM 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 (COT) and lyso-sphingomyelin 509 (LSM 509).

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
4. Wasserstein MP, Schuchman EH: Acid sphingomyelinase deficiency. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2006. Updated June 18, 2015. Accessed November 2, 2020. Available at www.ncbi.nlm.nih.gov/books/NBK1370/

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
6. Gal AE, Brady RO, Hibbert SR, Pentchev PG: A practical chromogenic procedure for the detection of homozygotes and heterozygous carriers of Niemann-Pick disease. N Engl J Med. 1975 Sep 25;293(13):632-636
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
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 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, Thursday

Report Available
2 to 7 days

Specimen Retention Time
2 months

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
OXNP	Oxysterols, P	92740-0

Result ID	Test Result Name	Result LOINC® Value
36430	Cholestane-3beta,5alpha,6beta-triol	92755-8
36431	7-Ketocholesterol	92764-0
36432	Lyso-sphingomyelin	92747-5
36433	Interpretation (OXNP)	59462-2
36434	Reviewed By	18771-6