Test Definition: OXNP

Oxysterols, Plasma

Overview

Useful For

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

Monitoring of individuals with Niemann-Pick type C disease

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

Testing Algorithm

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

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)

Special 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

Plasma

Ordering Guidance

This test is also available as a part of a panel; see HSMP / Hepatosplenomegaly Panel, Plasma. If this test (OXNP) is ordered with either GPSYP / Glucopsychosine, Plasma or CTXP / Cerebrotendinous Xanthomatosis, Plasma, the individual tests will be canceled and HSMP ordered.

Specimen Required

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
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. **Do not 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	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.

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, 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 patients 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 (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 neonates 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. Individuals with NPC exhibit elevated levels of oxysterol COT; LSM 509 and7-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. 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 is highly suggestive of Niemann-Pick disease type C (NPC).

An elevation of lyso-sphingomyelin is highly suggestive of Niemann-Pick 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

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
9. Mengel E, Patterson MC, Da Riol RM, et al. Efficacy and safety of arimoclomol in Niemann-Pick disease type C: Results from a double-blind, randomised, placebo-controlled, multinational phase 2/3 trial of a novel treatment. J Inherit Metab Dis. 2021;44(6):1463-1480. doi:10.1002/jimd.12428

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 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
2 months

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
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