Overview

Useful For
Investigation of possible diagnoses of Niemann-Pick disease types A, B, or C in plasma specimens
Monitoring of individuals with NPC disease

Testing Algorithm
The following are available in 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

Special Instructions
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Method Name
Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Plasma

Specimen Required
Collection Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Sodium heparin, lithium heparin, or ACD B

Submission Container/Tube: Plastic vial

Specimen Volume: 0.3 mL

Forms
If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume
0.25 mL

Reject Due To

| Gross hemolysis | OK |

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

Niemann-Pick disease types A and B are caused by a deficiency of sphingomyelinase which results in extensive storage of sphingomyelin and cholesterol in the liver, spleen, lungs, and, to a lesser degree, brain. Niemann-Pick type A disease is more severe than type B and characterized by early onset with feeding problems, dystrophy, persistent jaundice, development of hepatosplenomegaly, neurological deterioration, deafness, and blindness leading to death by age 3. Niemann-Pick type B 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 \( \text{SMPD1} \) 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 mutations in the \( \text{SMPD1} \) gene. Although there is a higher frequency of type A among the Ashkenazi Jewish population, both types are pan-ethnic. Individuals with NPD types A and B typically have elevation of the oxysterol lyso-sphingomyelin (LSM), lyso-sphingomyelin 509 (LSM 509), cholestane-3 beta, 5 alpha, 6 beta-triol and/or 7-ketocholesterol (7-KC) may also be elevated. Molecular genetic testing for NPA and NPB disease is also available (see NPABZ / Niemann-Pick Disease, Types A and B, Full Gene Analysis).

Niemann-Pick disease type C (NPC)(1) is caused by a defect in cellular cholesterol trafficking that results in the progressive accumulation of unesterified cholesterol in late endosomes/lysosomes. 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 mutations in either the \( \text{NPC1} \) or \( \text{NPC2} \) 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 (see NPCZ / Niemann-Pick Type C Disease, Full Gene Analysis).
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
This test is not suitable for the identification of carriers.

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


### 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 (MRM) 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) and Time(s) Test Performed

Tuesday; 8 a.m.

#### Analytic Time

2 days (not reported on Saturday or Sunday)

#### Maximum Laboratory Time

8 days

#### Specimen Retention Time

2 months

#### Performing Laboratory Location

Rochester

#### Fees and 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 U.S. Food and Drug Administration.

#### CPT Code Information
## Test Definition: OXNP

**Oxysterols, P**

### LOINC® Information

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