# Test Definition: OXYBS

Oxysterols, Blood Spot

## Overview

### Useful For

Investigating a possible diagnosis of acid sphingomyelinase deficiency, also known as Niemann-Pick disease type A or B, using dried blood spots

This test is **not recommended** for diagnosis of Niemann-Pick type C (NPC) disease. If NPC is suspected, consider plasma oxysterols.

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

### Testing Algorithm

If the patient has abnormal newborn screening results for acid sphingomyelinase deficiency, also called Niemann- Pick type A or B 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

Based on internal validation studies, this test using dried blood spots is less clinically sensitive and specific for diagnosing Niemann-Pick type C (NPC) (75% and 89%, respectively) than using plasma (98%). If there is a strong clinical suspicion for NPC, order 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 | Reject |
| Insufficient specimen | Reject |
| Layering | Reject |
| 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 lyso-sphingomyelin is highly suggestive of acid sphingomyelinase deficiency, also called Niemann-Pick type A or B disease.

An elevation of cholestane-3-beta, 5-alpha, 6-beta-triol is highly suggestive of Niemann-Pick type C 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 16, 2025. 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 16, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1370/
3. 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.
4. Hollak CE, de Sonnaville ES, 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
5. 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

## 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, Thursday

### Report Available
3 to 7 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 |