Overview

Useful For
Evaluation of patients with a clinical presentation suggestive of a lysosomal storage disorder, specifically Gaucher, Niemann-Pick type A or type B, Pompe, Krabbe, Fabry disease, or mucopolysaccharidosis I; or a peroxisomal disorder, either X-linked adrenoleukodystrophy or Zellweger syndrome spectrum

Highlights
This is a screening test performed from a blood spot for a select number of lysosomal and peroxisomal disorders, including Gaucher disease, Fabry disease, Pompe disease, Krabbe disease, Niemann-Pick diseases A and B, mucopolysaccharidosis type I, Zellweger syndrome spectrum, and X-linked adrenoleukodystrophy.

Additional biochemical or molecular testing is required to confirm a diagnosis if enzyme deficiency is detected by this screening test.

Reflex Tests

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<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<td>Psychosine, BS</td>
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<td>Glucopsychosine, BS</td>
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<td>Pompe Disease, BS</td>
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<tr>
<td>LGBBS</td>
<td>Globotriaosylsphingosine, BS</td>
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Testing Algorithm
Results will be reviewed and second tier testing (lysophosphatidylcholines, mucopolysaccharidosis, psychosine, glucopsychosine, globotriaosylsphingosine, oxysterols, or Supplemental Newborn Screen (SNS) for the calculated ratio of creatine:creatinine) may be performed at a clinical biochemical geneticist's discretion at an additional charge.

The following algorithms are available in Special Instructions:

- [Newborn Screen Follow-up for Gaucher Disease](#)
- [Newborn Screen Follow-up for Mucopolysaccharidosis Type I](#)
- [Newborn Screen Follow-up for Niemann Pick Type A and B](#)
- [Newborn Screen Follow-up for X-Linked Adrenoleukodystrophy](#)
- [Newborn Screen Follow-up for Fabry Disease](#)
- [Newborn Screen Follow-up for Pompe Disease](#)
Test Definition: PLSD
Lysosomal/Peroxisomal D/O Scrn, BS

- Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm

For more information, see the following Newborn Screening ACT Sheets in Special Instructions:

- Newborn Screening Act Sheet Fabry Disease: Decreased Alpha-Galactosidase A
- Newborn Screening Act Sheet Gaucher Disease: Decreased Acid Beta-Glucosidase
- Newborn Screening Act Sheet Krabbe Disease: Decreased Galactocerebrosidase
- Newborn Screening Act Sheet Mucopolysaccharidosis Type I: Decreased Alpha-L-Iduronidase
- Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase
- Newborn Screening Act Sheet X-linked Adrenoleukodystrophy: Increased Very Long Chain Fatty Acids
- Newborn Screening Act Sheet Pompe Disease: Decreased Acid Alpha-Glucosidase

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screening Act Sheet Fabry Disease: Decreased Alpha-Galactosidase A
- Newborn Screening Act Sheet Gaucher Disease: Decreased Acid Beta-Glucosidase
- Newborn Screening Act Sheet Krabbe Disease: Decreased Galactocerebrosidase
- Newborn Screening Act Sheet Mucopolysaccharidosis Type I: Decreased Alpha-L-Iduronidase
- Newborn Screening Act Sheet Niemann-Pick A/B Disease: Decreased Acid Sphingomyelinase
- Newborn Screening Act Sheet Pompe Disease: Decreased Acid Alpha-Glucosidase
- Newborn Screening Act Sheet X-linked Adrenoleukodystrophy: Increased Very Long Chain Fatty Acids

Method Name
Flow Injection Analysis-Tandem Mass Spectrometry (FIA-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Whole blood

Advisory Information
To evaluate adult patients with a clinical presentation suggestive of adrenomyeloneuropathy (AMN), the recommended test is POX / Fatty Acid Profile, Peroxisomal (C22-C26), Serum. Lysophosphatidylcholine (LPC) concentrations may not be consistently elevated in adult blood spots.

**Specimen Required**

**Supplies:** Card-Blood Spot Collection (Filter Paper) (T493)

**Container/Tube:**

**Preferred:** Card-Blood Spot Collection (Filter Paper) (T493)

**Acceptable:** Ahlstrom 226 filter paper, Munktell filter paper, Whatman Protein Saver 903 paper, or blood collected in tubes containing ACD, EDTA, or heparin and dried on acceptable filter paper

**Specimen Volume:** 2 blood spots

**Collection Instructions:**

1. Completely fill at least 2 circles on the filter paper card (approximately 100 microliters blood per circle).

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

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 in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

**Forms**

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)

2. **Biochemical Genetics Patient Information** (T602) in Special Instructions

3. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

   - General Request (T239)
- Inborn Errors of Metabolism Test Request (T798)
### Clinical and Interpretive

#### Clinical Information

Lysosomes are intracellular organelles that contain hydrolytic enzymes to degrade a variety of macromolecules. Lysosomal storage disorders are a diverse group of inherited diseases where macromolecules accumulate due to defects in their transport mechanisms across the lysosomal membrane or due to defective lysosomal enzyme function. Accumulation of these macromolecules in the lysosomes leads to cell damage and, eventually, organ dysfunction. More than 40 lysosomal storage disorders have been described with a wide phenotypic spectrum.

Gaucher disease is an autosomal recessive lysosomal storage disorder caused by a deficiency of acid beta-glucosidase (glucocerebrosidase: GBA) resulting in increased storage of glucocerebroside (D-glucosylceramide). The deposition of glucocerebroside in macrophages of the reticuloendothelial system (Gaucher cells) causes organ dysfunction and organomegaly. Gaucher cells, found in the spleen, bone marrow, lung, lymph nodes, and liver, are characteristic of the disease. There are 3 clinical types of Gaucher disease:

- **Type I**: adult/chronic
- **Type II**: acute neuropathic/infantile
- **Type III**: subacute neuropathic/juvenile

Type I, the most frequent form of the disease, is characterized by organomegaly, thrombocytopenia, and bone pain, and is frequent among the Ashkenazim. Hepatosplenomegaly is usually present in all 3 types. Involvement of the central nervous system (CNS) is limited to the infantile type (type II). Enzyme replacement therapy and/or substrate reduction therapy are available for patients with Gaucher disease type I.

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
Pompe disease, also known as glycogen storage disease type II, is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid alpha-glucosidase (GAA; acid maltase) due to mutations in the GAA gene. The estimated incidence is 1 in 40,000 live births. In Pompe disease, glycogen that is taken up by lysosomes during physiologic cell turnover accumulates, causing lysosomal swelling, cell damage, and, eventually, organ dysfunction. This leads to progressive muscle weakness, cardiomyopathy, and, ultimately, death. The clinical phenotype appears to be dependent on residual enzyme activity. Complete loss of enzyme activity causes onset in infancy leading to death, typically within the first year of life. Juvenile and adult-onset forms are characterized by later onset and longer survival with primary symptoms that include muscle weakness and respiratory insufficiency, though rarely, clinically significant cardiomyopathy can be seen. Since Pompe disease is considered a rare condition that progresses rapidly in infancy, the disease, when presenting as juvenile and adult-onset forms, is often diagnosed late, if at all, during the evaluation of patients presenting with muscle hypotonia, weakness, or cardiomyopathy. Treatment with enzyme replacement therapy is available and improves prognosis, making early diagnosis of Pompe disease desirable.

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive disorder caused by a deficiency of galactocerebrosidase (GALC, galactosylceramide beta-galactosidase). Galactosylceramide (as with sulfated galactosylceramide) is a lipid component of myelin. The absence of GALC results in globular, distended, multinucleated bodies in the basal ganglia, pontine nuclei, and cerebral white matter. There is severe demyelination throughout the brain with progressive cerebral degenerative disease affecting primarily the white matter. Severely affected individuals typically present between 3 to 6 months of age with increasing irritability and sensitivity to stimuli. Rapid neurodegeneration including white matter disease follows with death usually occurring by age 2. A subset of individuals has later onset forms of the disease that are characterized by ataxia, vision loss, weakness, and psychomotor regression. They can present anywhere from age 6 months to the seventh decade of life, and based on newborn screening experience in New York, appear to be more common than the earlier onset variants. The clinical course of Krabbe disease can be variable, even within the same family. Of note, Krabbe disease variants, including pseudodeficiency, are not distinguishable by enzyme activity measurement. Hematopoietic stem cell transplantation, particularly when performed within the first few weeks of life, is a treatment option with potential benefit.

Fabry disease is an X-linked recessive disorder with an incidence of approximately 1 in 50,000 males. Symptoms result from a deficiency of the enzyme alpha-galactosidase A (GLA; ceramide trihexosidase). Reduced GLA activity results in accumulation of glycosphingolipids in the lysosomes of both peripheral and visceral tissues. Severity and onset of symptoms are dependent on the residual GLA activity. Males with less than 1% GLA activity have the classic form of Fabry disease. Symptoms can appear in childhood or adolescence and usually include acroparesthesias (pain crises), multiple angiokeratomas, reduced or absent sweating, and corneal opacity. Renal insufficiency, leading to end-stage renal disease and cardiac and cerebrovascular disease, generally occurs in middle age. Males with residual a-Gal A activity greater than1% may present with one of 3 variant forms of Fabry disease with onset of symptoms later in life: a renal variant associated with end stage renal disease (ESRD) but without the pain or skin lesions, a cardiac variant typically presenting in the sixth to eighth decade with left ventricular hypertrophy, cardiomyopathy and arrhythmia, and proteinuria, but without ESRD, and a cerebrovascular variant presenting as stroke or transient ischemic attack. The variant forms of Fabry disease may be underdiagnosed. Females who are carriers of Fabry disease can have clinical presentations ranging from asymptomatic to severely affected. Enzyme replacement therapy is a treatment option for Fabry disease.

Mucopolysaccharidosis I (MPS I) is an autosomal recessive disorder caused by a reduced or absent activity of the alpha-L-iduronidase enzyme. Deficiency of the alpha-L-iduronidase enzyme can result in a wide range of phenotypes further categorized into 3 syndromes: Hurler syndrome (MPS IH), Scheie syndrome (MPS IS), and Hurler-Scheie syndrome (MPS IH/S). Because there is no way to distinguish the syndromes biochemically, they are also referred to as MPS I and attenuated MPS I. Clinical features and severity of symptoms of MPS I are widely variable, ranging from severe disease to an attenuated form that generally presents at a later onset with a milder clinical presentation. In general, symptoms may include coarse facies, progressive dysostosis multiplex, hepatosplenomegaly, corneal
clouding, hearing loss, mental retardation or learning difficulties, and cardiac valvular disease. The incidence of MPS I is approximately 1 in 100,000 live births. Treatment options include hematopoietic stem cell transplantation and enzyme replacement therapy.

Peroxisomal disorders include 2 major subgroups: disorders of peroxisomal biogenesis and single peroxisomal enzyme/transporter defects. Peroxisomes are organelles present in all human cells except mature erythrocytes. They carry out essential metabolic functions including beta-oxidation of very long-chain fatty acids (VLCFA), alpha-oxidation of phytanic acid, and biosynthesis of plasmalogen and bile acids. Peroxisome biogenesis defects such as Zellweger spectrum disorders are characterized by defective assembly of the entire organelle, whereas in single enzyme/transporter defects such as X-linked adrenoleukodystrophy, the organelle is intact, but a specific function is disrupted. These disorders are clinically diverse and range in severity from neonatal lethal to milder, later onset variants.

Zellweger syndrome spectrum (ZSS) is a continuum of severe disorders affecting the nervous system, vision, hearing, and liver function. Most individuals present in infancy, but adult patients have been identified. The prevalence of ZSS is 1 in 50,000. ZSS follows autosomal recessive inheritance. At least 12 different genes have been implicated in ZSS, with approximately 60% to 70% of mutations occurring in PEX1. The clinical phenotypes include Zellweger syndrome, neonatal adrenoleukodystrophy (NALD), and infantile Refsum disease (IRD). Individuals with Zellweger syndrome typically die within the first year of life without making any developmental progress. Individuals with NALD or IRD typically present in childhood with developmental delays, vision loss, and hearing loss, and have a much slower disease progression. There is no specific treatment for ZSS.

X-linked adrenoleukodystrophy (XALD) is a disorder affecting the nervous system, adrenal cortex, and testis. It is the most common of the peroxisomal disorders, affecting 1 in 17,000 to 1 in 21,000 males. A defect in the ABCD1 gene is responsible for the disease. X-ALD shows a wide range of phenotypic expressions. The clinical phenotypes occurring in males can be subdivided in 4 main categories: cerebral inflammatory, adrenomyeloneuropathy (AMN), Addison only, and asymptomatic. The first 2 phenotypes account for almost 80% of the patients, while the frequency of the asymptomatic category diminishes with age and it is very rare after age 40. It is estimated that approximately 50% of heterozygotes are symptomatic and develop an AMN-like syndrome. Treatment options are hormone replacement therapy, dietary intervention, or hematopoietic stem cell transplantation.

### Reference Values

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<th>Disease</th>
<th>Marker</th>
<th>Normal Range</th>
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<td>Gaucher</td>
<td>Acid Beta-Glucosidase</td>
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<td>Niemann-Pick A/B</td>
<td>Sphingomyelinase</td>
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<td>NA</td>
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### Interpretation

An interpretive report will be provided.
When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro confirmatory studies (enzyme assay, molecular analysis), name and phone number of key contacts who may provide these studies at Mayo Clinic Laboratories or elsewhere, and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on the analysis, independent biochemical (eg, in vitro enzyme assay) or molecular genetic analyses are required.

Cautions
A positive test result is strongly suggestive of a diagnosis but needs follow-up by stand-alone biochemical or molecular assay.

Clinical Reference


Performance

Method Description
Two 1/8-inch dried blood spots (DBS) are excised from a single specimen. The enzymes are extracted by incubating the specimens with a mix of substrate and internal standard for acid sphingomyelinase (ASM), beta-glucocerebrosidase (ABG), alpha-glucosidase (GAA), alpha-galactosidase (GLA), galactocerebrosidase (GALC) and alpha-L-iduronidase (IDUA). The sample is then purified by liquid-liquid extraction. The second DBS is extracted with methanol containing d4-C26 LPC. The resulting extracts are then combined, evaporated and reconstituted before analysis by tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Sunday; 11:30 a.m.

Analytic Time
2 days
Maximum Laboratory Time
16 days

Specimen Retention Time
1 year

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
83789

LOINC® Information

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