MAYO CLINIC LABORATORIES

Test Definition: PLSD

Lysosomal and Peroxisomal Disorders Screen, Blood Spot

Overview

Useful For

Evaluation of patients with a clinical presentation suggestive of a lysosomal disorder, specifically Gaucher, infantile neurovisceral or chronic visceral acid sphingomyelinase deficiency, Pompe, Krabbe, or Fabry disease, or mucopolysaccharidosis I or II; or a peroxisomal disorder, either X-linked adrenoleukodystrophy or Zellweger spectrum disorders

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
MPSBS	Mucopolysaccharidosis, BS	Yes	No
PSY	Psychosine, BS	Yes	No
GPSY	Glucopsychosine, BS	Yes	No
OXYBS	Oxysterols, BS	Yes	No
LPCBS	LysoPC by LC MS/MS, BS	Yes	No
PDBS	Pompe Disease, BS	Yes	No
LGBBS	Globotriaosylsphingosine, BS	Yes	No

Testing Algorithm

First-tier results will be reviewed, and second-tier screening performed at a clinical biochemical geneticist's discretion at an additional charge. This minimizes the false-positive rate and maximizes the positive predictive value of screening for these disorders.

For more information see:
Newborn Screen Follow up for Fabry Disease
Newborn Screen Follow-up for Gaucher Disease
Newborn Screen Follow-up for Mucopolysaccharidosis Type I Decreased Alpha-L-Iduronidase Activity
Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans
Newborn Screen Follow-up for Pompe Disease
Newborn Screen Follow-up for X-Linked Adrenoleukodystrophy

If the patient has abnormal newborn screening results for X-linked adrenoleukodystrophy or a lysosomal disorder, immediate actions should be taken. Refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1)

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions

- Newborn Screen Follow-up for X-Linked Adrenoleukodystrophy
- Newborn Screen Follow-up for Pompe Disease
- Newborn Screen Follow-up for Mucopolysaccharidosis Type I Decreased Alpha-L-Iduronidase Activity
- Newborn Screen Follow-up for Gaucher Disease
- Blood Spot Collection Card-Chinese Instructions
- Newborn Screen Follow up for Fabry Disease
- Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions
- Newborn Screen Follow-up for Acid Sphingomyelinase Deficiency
- Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

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 and II, Zellweger spectrum disorders, and X-linked adrenoleukodystrophy.

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

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

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

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Blood Spot Collection Card
Acceptable: PerkinElmer 226 filter paper, Munktell filter paper, Whatman Protein Saver 903 paper, local newborn screening card, or blood collected in tubes containing ACD or EDTA and dried on acceptable filter paper

Specimen Volume: 2 Blood spots

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. Completely fill at least 2 circles on the filter paper card (approximately 100 microliters blood per circle).
3. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. 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

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. 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

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Specimens known to have been exposed to elevated temperatures above ambient	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	90 days	FILTER PAPER
	Ambient	28 days	FILTER PAPER
	Frozen	90 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

Lysosomes are intracellular organelles that contain hydrolytic enzymes to degrade a variety of macromolecules. Lysosomal disorders are a diverse group of inherited diseases where macromolecules accumulate due to either defects in their transport mechanisms across the lysosomal membrane or defective lysosomal enzyme function. Accumulation of these macromolecules in the lysosomes leads to cell damage and, eventually, organ dysfunction. More than 50 lysosomal disorders have been described with a wide phenotypic spectrum.

Gaucher disease results from a deficiency of the enzyme, beta-glucosidase, due to disease-causing variants in the *GBA1* gene. Beta-glucosidase facilitates the lysosomal degradation of glucosylceramide (glucocerebroside) and glucopsychosine (glucosylsphingosine). There are 3 described types of Gaucher disease with varying clinical presentations and age of onset, from a perinatal lethal disorder to milder, later onset variants. Features of all types of Gaucher disease include hepatosplenomegaly and hematological abnormalities. Treatment is available in the form of enzyme replacement therapy (ERT), substrate reduction therapy, and chaperone therapy for types 1 and 3. Currently, only supportive therapy is available for type 2.

Acid sphingomyelinase deficiency (ASMD) is an autosomal recessive disorder caused by disease-causing variants in the *SMPD1* gene. This results in extensive storage of sphingomyelin and cholesterol in the liver, spleen, lungs, and, to a lesser degree, brain. An early-onset form, infantile neurovisceral ASMD (historically known as Niemann-Pick type A) is characterized by early onset feeding problems, dystrophy, persistent jaundice, development of hepatosplenomegaly, neurological deterioration, deafness, and blindness leading to death by 3 years of age. A later-onset, chronic visceral form of ASMD (historically known as Niemann-Pick type B) 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. Treatment is available in the form of ERT to help reduce the accumulation of sphingomyelin in the lung, liver, spleen, and other non-central nervous system organs. ERT does not impact the central nervous system.

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 disease-causing variants 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. The clinical presentation of Pompe disease ranges from a rapidly progressive infantile form, which is lethal if untreated, to a more slowly progressive late onset form. All disease variants are eventually associated with progressive muscle weakness and respiratory insufficiency. Cardiomyopathy is associated almost exclusively with the infantile form. ERT is available for all disease forms and should be started as soon as possible for patients with the infantile form and at the first signs of muscle disease in the later onset forms.

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive disorder caused by disease-causing variants in the *GALC* gene resulting in 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 with increasing irritability and sensitivity to stimuli. Rapid neurodegeneration, including white matter disease, follows with death usually occurring by 2 to 5 years. A subset of individuals have later onset forms of the disease, which 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. Psychosine has been shown to be elevated in patients with clinical signs and symptoms of disease and, therefore, may be a useful biomarker for the presence of disease or disease progression. The only available therapy is hematopoietic stem cell transplantation (HSCT), which is best performed prior to the onset of clinical symptoms. Infantile Krabbe disease must, therefore, be considered a critical, time-sensitive newborn screening condition.

Fabry disease is an X-linked disorder caused by disease-causing variants in the *GLA* gene resulting in a deficiency of the alpha-galactosidase A (GLA) enzyme. 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. Male patients with (near) absent 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 kidney disease and cardiac and cerebrovascular disease, generally occurs in middle age. Male patients with residual GLA activity may present with a variant form of Fabry disease with onset of symptoms later in life. The renal variant generally has onset of symptoms in the third decade. The most prominent feature is renal insufficiency and, ultimately, end stage kidney disease. Individuals with the renal variant may or may not share other symptoms with the classic form of Fabry disease. Individuals with the cardiac variant are often asymptomatic until they present with cardiomyopathy or mitral insufficiency in the fourth decade. The cardiac variant is not associated with kidney failure. Female patients with Fabry disease can have clinical presentations ranging from asymptomatic to severely affected. ERT is a treatment option for all patients with Fabry disease.

Mucopolysaccharidosis I (MPS I) is an autosomal recessive disorder caused by a reduced or absent activity of the alpha-L-iduronidase (IDUA) enzyme. Reduced IDUA activity results in accumulation of glycosaminoglycans (mucopolysaccharides) within the lysosome. The clinical presentation and severity of symptoms of MPS I are variable, ranging from severe disease to attenuated variants (historically known as Hurler-Scheie disease and Scheie disease) that generally present with a later onset and a milder clinical presentation. In general, symptoms may include coarse facies, progressive dysostosis multiplex, hepatosplenomegaly, corneal clouding, hearing loss, intellectual disability or learning difficulties, and cardiac valvular disease. MPS I is caused by disease-causing variants in the *IDUA* gene. Treatment options include HSCT and ERT.

Mucopolysaccharidosis II (MPS II; Hunter syndrome) is an X-linked disorder caused by the deficiency of iduronate 2-sulfatase (I2S) enzyme due to disease-causing variants in the *IDS* gene. Reduced I2S activity results in accumulation of glycosaminoglycans (mucopolysaccharides) within the lysosome. Clinical features and severity of symptoms are widely variable ranging from severe infantile onset disease to an attenuated form, which generally has a later onset with a milder clinical presentation. Symptoms may include coarse facies, short stature, enlarged liver and spleen, hoarse voice, stiff joints, cardiac disease, and profound neurologic involvement leading to developmental delays and regression. As an

X-linked disorder, MPS II occurs primarily in male patients with an estimated incidence of 1 in 120,000 male births, although symptomatic carrier females have been reported. Treatment options include HSCT and ERT.

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, alpha-oxidation of phytanic acid, and biosynthesis of plasmalogen and bile acids. Peroxisomal disorders include 2 major subgroups: disorders of peroxisomal biogenesis and single peroxisomal enzyme/transporter defects. Peroxisome biogenesis defects, such as Zellweger spectrum disorders (ZSD) are characterized by defective assembly of the entire organelle, whereas in single enzyme/transporter defects such as X-linked adrenoleukodystrophy (XALD), 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.

X-linked adrenoleukodystrophy is an X-linked disorder affecting the nervous system, adrenal cortex, and testis. It is the most common of the peroxisomal disorders. XALD is caused by a disease-causing variant in the *ABCD1*. XALD shows a wide range of phenotypic expressions. The clinical phenotypes occurring in male patients 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 is very rare after age 40. It is estimated that approximately 65-80% of heterozygous individuals develop symptoms of an AMN-like phenotype. Treatment options include hormone replacement therapy, HSCT, gene therapy, or symptom management.

Zellweger spectrum disorders are a continuum of severe disorders affecting the nervous system, vision, hearing, and liver function. Most affected individuals present in childhood, but adult patients have been identified. Most ZSDs are inherited in an autosomal recessive pattern. At least 13 different genes have been implicated in ZSD, with approximately 60% to 70% of variants occurring in *PEX1*. The clinical phenotypes include Zellweger syndrome, neonatal adrenoleukodystrophy (NALD), and infantile Refsum disease (IRD). The phenotypic spectrum and disease severity is broad. There is no specific treatment for ZSD.

Reference Values

Disease	Marker	Normal range
Gaucher	Acid beta-glucosidase	> or =1.75 nmol/mL/hr
Niemann-Pick A/B	Sphingomyelinase	> or =2.5 nmol/mL/hr
Pompe	Acid alpha-glucosidase	> or =3.0 nmol/mL/hr
Krabbe	Galactocerebrosidase	> or =0.4 nmol/mL/hr
Fabry	Alpha-galactosidase	> or =2.00 nmol/mL/hr
MPS I	Alpha-L-iduronidase	> or =1.5 nmol/mL/hr
MPS II	Iduronate 2-sulfatase	> or =4.0 nmol/mL/hr
NA	C20 Lysophosphatidylcholine	< or =1.81 nmol/mL
NA	C22 Lysophosphatidylcholine	< or =0.43 nmol/mL
ALD/PBD/ALDH	C24 Lysophosphatidylcholine	< or =0.49 nmol/mL
ALD/PBD/ALDH	C26 Lysophosphatidylcholine	< or =0.47 nmol/mL

Interpretation

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), 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 requires follow-up by either a stand-alone biochemical or molecular assay.

Carrier status (heterozygosity) for these conditions cannot be reliably detected.

Iduronate-2-sulfatase can also be deficient in individuals with multiple sulfatase deficiency.

Clinical Reference

1. Newborn Screening ACT Sheets. American College of Medical Genetics and Genomics. Accessed October 2, 2025. Available at www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx?hkey=9d6bce5a-182e-42a6-84a5-b2d88240c508
2. Reuser AJ, Verheijen FW, Bali D, et al. The use of dried blood spot samples in the diagnosis of lysosomal storage disorders--current status and perspectives. Mol Genet Metab. 2011;104(1-2):144-148. doi:10.1016/j.ymgme.2011.07.014
3. Klouwer FCC, Ferdinandusse S, van Lenthe H, et al. Evaluation of C26:0-lysophosphatidylcholine and C26:0-carnitine as diagnostic markers for Zellweger spectrum disorders. J Inherit Metab Dis. 2017;40(6):875-881. doi:10.1007/s10545-017-0064-0
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5. Part 15 Peroxisomes. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed October 2, 2025. Available at https://ommbid.mhmedical.com/book.aspx?bookid=2709#225069419
6. Part 16 Lysosomal disorders. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed October 2, 2025. Available at https://ommbid.mhmedical.com/book.aspx?bookid=2709#225069419

Performance

Method Description

Three 1/8-inch dried blood spots (DBS) are excised from a single specimen. The enzymes are extracted from 2 DBS by incubating the specimens with a mix of substrate and internal standard for acid sphingomyelinase,

beta-glucocerebrosidase, alpha-glucosidase, alpha-galactosidase, galactocerebrosidase, alpha-L-iduronidase, and iduronate 2-sulfatase. The sample is then purified by liquid-liquid extraction. The third DBS is extracted with methanol containing d4-C26 lysophosphatidylcholine. The resulting extracts are then combined, evaporated, and reconstituted before analysis by tandem mass spectrometry.(Tortorelli S, Turgeon C, Gavrilov D, et al. Simultaneous testing for 6 lysosomal storage disorders and X-adrenoleukodystrophy in dried blood spots by tandem mass spectrometry. Clin Chem. 2016;62[9]:1248-1254)

PDF Report
No

Day(s) Performed
Monday through Sunday

Report Available
2 days

Specimen Retention Time
6 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
83789

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PLSD	Lysosomal/Peroxisomal D/O Scrn, BS	105458-4

Result ID	Test Result Name	Result LOINC® Value
34811	Acid Beta-Glucosidase	55917-9

34812	Sphingomyelinase	62316-5
34813	Acid Alpha-Glucosidase	55827-0
34814	Galactocerebrosidase	62310-8
34815	Alpha-Galactosidase	55908-8
34816	Alpha-L-Iduronidase	55909-6
34817	C20 Lysophosphatidylcholine	90920-0
34818	C22 Lysophosphatidylcholine	90921-8
34819	C24 Lysophosphatidylcholine	90922-6
34820	C26 Lysophosphatidylcholine	90923-4
34821	Interpretation (PLSD)	62301-7
34822	Reviewed By	18771-6
620785	Iduronate 2-Sulfatase	79462-8