Test Definition: LSD6W

Lysosomal Disorders, Six-Enzyme Panel, Leukocytes

Overview

Useful For

Diagnosis of the lysosomal disorders: Fabry (in male patients), Gaucher, Krabbe, mucopolysaccharidosis I (MPS I), acid sphingomyelinase deficiency (Niemann-Pick types A and B), and Pompe (glycogen storage disorder type II)

This test is **not intended for** carrier detection.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
GAAWR	Acid Alpha-Glucosidase Reflex, WBC	Yes, (Order GAAW)	No
GALCR	Galactocerebrosidase Reflex, WBC	Yes, (Order GALCW)	No

Genetics Test Information

Lysosomal disorders are a diverse group of inherited diseases characterized by the intracellular accumulation of macromolecules leading to cell damage and organ dysfunction.

Due to the improved outcomes associated with presymptomatic intervention, some states have added select lysosomal disorders to their newborn screening programs.

This test is an enzyme testing panel for individuals with positive newborn screen results or clinical signs and symptoms suspicious for Fabry disease, Gaucher disease, Krabbe disease, mucopolysaccharidosis I, acid sphingomyelinase deficiency (Niemann-Pick A/B disease), or Pompe disease. If an enzyme deficiency is detected by this screening test, additional biochemical or molecular testing is required to confirm a diagnosis.

Testing Algorithm

If acid alpha-glucosidase is less than 5.00 nmol/hour/mg protein, then acid alpha-glucosidase will be added and performed at an additional charge.

If galactocerebrosidase is less than 1.88 nmol/hour/mg protein, then galactocerebrosidase will be added and performed at an additional charge.

If the patient has abnormal newborn screening results, refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1)

For more testing information see:
-Newborn Screen Follow-up for Acid Sphingomyelinase Deficiency
-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 Screen Follow-up for Pompe Disease
-Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase
-Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- 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
- Newborn Screen Follow up for Fabry Disease
- Informed Consent for Genetic Testing (Spanish)
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine
- Newborn Screen Follow-up for Acid Sphingomyelinase Deficiency

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole Blood ACD

Ordering Guidance

Carrier detection using enzyme levels is unreliable for female patients with Fabry disease as results may be within the normal values. Order GLA / Fabry Disease, GLA Gene Sequencing with Deletion/Duplication, Varies for testing carrier status.

Shipping Instructions

For optimal isolation of leukocytes, it is recommended the specimen arrives refrigerated within 6 days of collection to be stabilized. Collect specimen Monday through Thursday only and not the day before a holiday. Specimen should be collected and packaged as close to shipping time as possible.

Specimen Required

Container/Tube:

Preferred: Yellow top (ACD solution B)

Acceptable: Yellow top (ACD solution A) or lavender top (EDTA)

Specimen Volume: 6 mL

Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot**.

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

4 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD	Refrigerated (preferred)	6 days	
	Ambient	6 days	

Clinical & Interpretive

Clinical Information

Note: Where applicable, verbiage refers to sex assigned at birth.

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

Gaucher Disease:
Gaucher disease is an autosomal recessive lysosomal disorder caused by a deficiency of the enzyme, acid beta-glucosidase (glucocerebrosidase) due to variants in the *GBA* gene. Beta-glucosidase facilitates the lysosomal degradation of glucosylceramide (glucocerebroside) and glucopsychosine (glucosylsphingosine). Impaired enzyme activity results in accumulation of undegraded glucocerebrosides in the lysosome, resulting in 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 with varying presentations and age of onset but all include

hepatosplenomegaly and hematological abnormalities as symptoms. Gaucher disease type I is the most common, representing more than 90% of cases. It is generally characterized by bone disease, hepatosplenomegaly, anemia and thrombocytopenia, coagulation abnormalities, lung disease, but no central nervous system involvement. Gaucher disease types II and III are characterized by the presence of primary neurologic disease. In addition, type II typically presents with limited psychomotor development, hepatosplenomegaly, and lung disease, resulting in death usually between ages 2 and 4. Individuals with Gaucher disease type III may present prior to age 2, but the progression is not as rapid, and individuals may survive into the third and fourth decade of life. Treatment is available in the form of enzyme replacement therapy, substrate reduction therapy, and chaperone therapy for types 1 and 3 (type 3, subacute neuropathic/juvenile). Currently, only supportive therapy is available for type 2. The biomarker, glucopsychosine (GPSY / Glucopsychosine, Blood Spot), is elevated in symptomatic individuals and supports a diagnosis of Gaucher disease.

Acid Sphingomyelinase Deficiency, acute neurovisceral vs chronic visceral:
Historically known as Niemann-Pick disease types A and B, acid sphingomyelinase deficiency (ASMD), acute neurovisceral vs chronic visceral results in extensive storage of sphingomyelin and cholesterol in the liver, spleen, lungs, and, to a lesser degree, brain. ASMD, acute neurovisceral is more severe than the chronic visceral form and is characterized by early onset with feeding problems, dystrophy, persistent jaundice, development of hepatosplenomegaly, neurological deterioration, deafness, and blindness. Death typically occurs by age 3 years. ASMD, chronic visceral, affects many important internal organs, however, has little to no impact on neurologic function. It is more common than the acute form with survival into adulthood. Some individuals 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. ASMD is caused by variants in the *SMPD1* gene, and affected individuals typically have elevation of the oxysterol, lyso-sphingomyelin; cholestane-3 beta, 5 alpha, 6 beta-triol (COT) or 7-ketocholesterol (7-KC) may also be elevated. For more information see OXYBS / Oxysterols, Blood Spot.

Pompe Disease:
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 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 organ dysfunction. This leads to progressive muscle weakness, cardiomyopathy, and eventually, 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, as the names suggest, are characterized by later onset and longer survival. Because Pompe disease is considered a rare condition that progresses rapidly in infancy, the disease, in particular the juvenile and adult-onset forms, is often considered late, if at all, during the evaluation of individuals presenting with muscle hypotonia, weakness, or cardiomyopathy. Treatment with enzyme replacement therapy is available making early diagnosis of Pompe disease desirable, as early initiation of treatment may improve prognosis.

Krabbe Disease:
Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive disorder caused by a deficiency of the enzyme, galactocerebrosidase (GALC), due to variants in the *GALC* gene. GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates (galactosylceramide, lactosylceramide, and lactosylsphingosine). In individuals with Krabbe disease, reduced GALC activity results in impaired degradation of these substrates, causing severe demyelination throughout the brain with progressive cerebral degenerative disease affecting primarily the white matter. Severely affected individuals typically present between ages 3 to 6 months with increasing irritability and

sensitivity to stimuli. Rapid neurodegeneration including white matter disease follows with death usually occurring by age 2 years. Juvenile- and adult-onset variants present later in life, progress more slowly, and based on newborn screening experience in New York, appear to be more common than the earlier onset variants. Of note, Krabbe disease variants, including pseudodeficiency, may not be discriminated by enzyme activity measurement. Hematopoietic stem cell transplantation, particularly when performed within the first few weeks of life, has shown variable benefit. Although rare, a few infants with an early onset Krabbe disease phenotype due to deficiency of saposin A have been found. Saposin A is a sphingolipid activator protein that assists galactocerebrosidase in its action on galactosylceramide. The biomarker, psychosine (PSY / Psychosine, Blood Spot) has been shown to be elevated in individuals with active Krabbe disease.

Fabry Disease:
Fabry disease, caused by variants in the *GLA* gene, is an X-linked recessive disorder with an incidence of approximately 1 in 50,000 male patients. 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. Male patients 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. Kidney insufficiency, leading to end-stage kidney disease, and cardiac and cerebrovascular disease, generally occurs in middle age. Male patients with more than 1% GLA activity may present with a variant form of Fabry disease. The kidney variant generally has onset of symptoms in the third decade. The most prominent feature in this form is kidney insufficiency and, ultimately, end-stage kidney disease. Individuals with this 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 cardiac findings such as cardiomyopathy or mitral insufficiency in the fourth decade. The cardiac variant is not associated with kidney failure. Female patients who are carriers of Fabry disease can have clinical presentations ranging from asymptomatic to severely affected. Measurement of GLA activity is not useful for identifying female patients with Fabry disease, as many carriers have normal enzyme activity. Additional studies including molecular genetic analysis of the *GLA* gene (GLA / Fabry Disease, GLA Gene Sequencing with Deletion/Duplication, Varies) are recommended to detect carriers. The biomarkers globotriaosylsphingosine (LGBBS / Globotriaosylsphingosine, Blood Spot) and ceramide trihexosides (CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine) may be elevated in individuals with Fabry disease and may aid in the diagnostic evaluation of female patients.

Mucopolysaccharidosis I:
Mucopolysaccharidosis I (MPS I) is an autosomal recessive disorder caused by a reduced or absent activity of the alpha-L-iduronidase enzyme. The mucopolysaccharides, heparan sulfate and dermatan sulfate, are elevated in affected individuals (MPSBS / Mucopolysaccharidosis, Blood Spot) and support a diagnosis of MPS I. 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, intellectual disabilities or learning difficulties, and cardiac valvular disease. MPS I is caused by variants in the *IDUA* gene and has an estimated incidence of approximately 1 in 100,000 live births. Treatment options include hematopoietic stem cell transplantation and enzyme replacement therapy.

Reference Values

Beta-Glucosidase: > or =2.88 nmol/hour/mg protein
Acid Sphingomyelinase: > or =0.32 nmol/hour/mg protein
Acid Alpha-Glucosidase: > or =5.00 nmol/hour/mg protein
Galactocerebrosidase: > or =1.88 nmol/hour/mg protein
Alpha-Galactosidase: > or =10.32 nmol/hour/mg protein
Alpha-L-Iduronidase: > or =2.06 nmol/hour/mg protein
Acid Alpha-Glucosidase (Reflex): > or =1.500 nmol/hour/mg protein
Galactocerebrosidase (Reflex): > or =0.300 nmol/hour/mg protein

An interpretative report will be provided.

Interpretation

Values below the reference ranges are consistent with a diagnosis of lysosomal disorders.

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, and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Cautions

Individuals with pseudodeficiency alleles can show reduced enzyme activity with this assay.

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

Enzyme levels may be normal in individuals receiving enzyme replacement therapy or who have undergone hematopoietic stem cell transplant.

Clinical Reference

1. Newborn Screening ACT Sheets. American College of Medical Genetics and Genomics; Accessed July 22, 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. Elliott S, Buroker N, Cournoyer JJ, et al. Pilot study of newborn screening for six lysosomal storage diseases using Tandem Mass Spectrometry. Mol Genet Metab. 2016;118(4):304-309
3. Matern D, Gavrilov D, Oglesbee D, Raymond K, Rinaldo P, Tortorelli S. Newborn screening for lysosomal storage disorders. Semin Perinatol. 2015;39(3):206-216
4. Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. Lysosomal disorders. In: The Online Metabolic and Molecular Bases of Inherited Disease (OMMBID). Part 16. McGraw-Hill; 2019. Accessed July 22, 2025. Available at https://ommbid.mhmedical.com/book.aspx?bookID=2709#2250694196
5. Liao HC, Spacil Z, Ghomashchi F, et al. Lymphocyte galactocerebrosidase activity by LC-MS/MS for post-newborn screening evaluation of Krabbe disease. Clin Chem. 2017;63(8):1363-1369
6. Lin N, Huang J, Violante S, et al. Liquid chromatography-tandem mass spectrometry assay of leukocyte acid

alpha-glucosidase for post-newborn screening evaluation of Pompe disease. Clin Chem. 2017;63(4):842-851

Performance

Method Description
The specimens are incubated with a mix of substrate and internal standard for acid sphingomyelinase, beta-glucocerebrosidase, acid alpha-glucosidase, alpha-galactosidase, galactocerebrosidase, and alpha-L-iduronidase. The sample is then purified by liquid-liquid extraction. The extract is evaporated and reconstituted before analysis by tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Preanalytical processing: Monday through Saturday.
Testing performed: Monday, Thursday

Report Available
2 to 10 days

Specimen Retention Time
White blood cell homogenate: 1 month

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
82657
82963
83789 (if appropriate for government payers)

82542 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LSD6W	Lysosomal (Six) Panel, WBC	94489-2

Result ID	Test Result Name	Result LOINC® Value
606172	Beta-Glucosidase	32540-7
606173	Acid Sphingomyelinase	24101-8
606178	Acid Alpha-Glucosidase	24051-5
606179	Acid Alpha-Glucosidase (Reflex)	94488-4
606174	Galactocerebrosidase	24084-6
606175	Galactocerebrosidase (Reflex)	94487-6
606176	Alpha-L-Iduronidase	24057-2
606177	Alpha-Galactosidase	24049-9
606180	Interpretation	59462-2
606181	Reviewed By	18771-6