Test Definition: PSYR

Psychosine, Whole Blood

Overview

Useful For

Aiding in the biochemical diagnosis of Krabbe disease using whole blood specimens

Follow-up of individuals affected with Krabbe disease

Follow-up testing after an abnormal newborn screening result for Krabbe disease

Monitoring of individuals at risk to develop late onset Krabbe disease

Monitoring of individuals with Krabbe disease after hematopoietic stem cell transplantation

Genetics Test Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal disorder caused by deficient activity of the enzyme galactocerebrosidase.

Krabbe disease is clinically variable; infantile-onset Krabbe disease is the most severe type, with rapid neurological regression resulting in early death.

Testing Algorithm

If the patient has abnormal newborn screening result for Krabbe disease, immediate action should be taken. Refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1,2)

Highlights

Elevations in psychosine support a diagnosis of Krabbe disease; therefore, psychosine quantitation is a useful biomarker in determining if an individual has active disease. In addition, psychosine quantitation in red blood cells may be a valuable biomarker to monitor disease progression or treatment response in individuals of all ages.

Psychosine may also be elevated in saposin A cofactor deficiency, which results in a similar clinical phenotype to Krabbe disease, but patients typically have normal galactocerebrosidase activity in vitro.

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This test is recommended for individuals of all ages, infancy through adulthood, for diagnosis or long-term monitoring of patients who have been treated or who are at risk of developing Krabbe disease.

If a result is needed within 24 hours, order PSY / Psychosine, Blood Spot.

Shipping Instructions

Must be sent refrigerated.

Necessary Information

1. Patient's age is required.

2. Date of hematopoietic stem cell transplantation (HSCT), if performed.

Specimen Required

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Green top (sodium heparin, lithium heparin)

Specimen Volume: 2 mL

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal disorder caused by deficient activity of the enzyme galactocerebrosidase (GALC). GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates, galactosylceramide, lactosylceramide, and lactosylsphingosine. Krabbe disease is caused by variants in the *GALC* gene, and it has an estimated frequency of 1 in 250,000 births.

The clinical course of Krabbe disease can be variable, even within the same family. Eighty-five percent to 90% of patients present before the first year of life with central nervous system impairment, including increasing irritability, developmental delay, and sensitivity to stimuli. Rapid neurodegeneration, including white matter disease follows, with

death usually occurring by 2 years of age. Late onset forms of the disease affect 10% to15% of individuals and are characterized by ataxia, vision loss, weakness, and psychomotor regression, typically presenting from age 6 months to the seventh decade of life.

Newborn screening for Krabbe disease has been implemented in some states. The early (presymptomatic) identification and subsequent testing of infants at risk for Krabbe disease may be helpful in reducing the morbidity and mortality associated with this disease. While treatment is mostly supportive, hematopoietic stem cell transplantation has shown some success if performed prior to onset of neurologic damage.

Psychosine is 1 of 4 substrates degraded by GALC and is a neurotoxin at elevated concentrations. It has been shown to be elevated in patients with active Krabbe disease or with saposin A cofactor deficiency and, therefore, may be a useful biomarker for the presence of disease or disease progression.

Reduced or absent GALC in leukocytes (GALCW / Galactocerebrosidase, Leukocytes) or dried blood spots (PLSD / Lysosomal and Peroxisomal Disorders Screen, Blood Spot) along with elevated psychosine levels can indicate a diagnosis of Krabbe disease. Molecular sequencing of the *GALC* gene (KRABZ / Krabbe Disease, Full Gene Analysis and Large [30 kb] Deletion, Varies) allows for detection of the disease-causing variants in affected patients and carrier detection in family members.

Individuals with a disease phenotype similar to Krabbe disease may have saposin A cofactor deficiency. Saposin A cofactor deficiency also results in elevated psychosine levels. Testing for this condition via molecular analysis of *PSAP* is useful in those with elevated psychosine and normal to moderately reduced GALC activity with normal molecular genetic *GALC* sequencing.

Reference Values

Normal <5 pmol/g Hb

Interpretation

An elevation of psychosine is indicative of Krabbe disease or saposin A cofactor deficiency.

Cautions

Individuals with later onset disease, such as adult-onset Krabbe disease, may have a normal psychosine result.

Clinical Reference

1. Newborn Screening ACT Sheet [Decreased galactocerebrosidase, elevated psychosine] Krabbe Disease (infantile form). American College of Medical Genetics and Genomics; 2021. Updated May 2022. Accessed June 10, 2024. Available at www.acmg.net/PDFLibrary/Krabbe-Infantile.pdf
2. Newborn Screening ACT Sheet [Decreased galactocerebrosidase, mildly elevated psychosine] Krabbe Disease (late-onset form). American College of Medical Genetics and Genomics; 2021. Updated May 2022. Accessed June 10, 2024. Available www.acmg.net/PDFLibrary/Krabbe-Later-Onset.pdf
3. Kwon JM, Matern D, Kurtzberg J, et al. Consensus guidelines for newborn screening, diagnosis and treatment of infantile Krabbe disease. Orphanet J Rare Dis. 2018;13(1):30. doi:10.1186/s13023-018-0766-x
4. Orsini JJ, Escolar ML, Wasserstein MP, et al. Krabbe disease. In: Adam MP, Mirzaa GM, Pagon R, eds. GeneReviews [Interntet]. University of Washington, Seattle; 2000. Updated October 11, 2018. Accessed August 31, 2023. Available at www.ncbi.nlm.nih.gov/books/NBK1238/
5. Turgeon CT, Orsini JJ, Sanders KA, et al. Measurement of psychosine in dried blood spots-a possible improvement to

newborn screening programs for Krabbe disease. J Inherit Metab Dis. 2015;38(5):923-929
6. Wenger DA, Escolar ML, Luzi P, Rafi MA. Krabbe disease (globoid cell leukodystrophy). In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed August 31, 2023. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546481&bookid=2709
7. Guenzel AJ, Turgeon CT, Nickander KK, et al. The critical role of psychosine in screening, diagnosis, and monitoring of Krabbe disease. Genet Med. 2020;22(6):1108-1118. doi:10.1038/s41436-020-0764-y
8. Thompson-Stone R, Ream MA, Gelb M, et al. Consensus recommendations for the classification and long-term follow up of infants who screen positive for Krabbe disease. Mol Genet Metab. 2021;134(1-2):53-59. doi:10.1016/j.ymgme.2021.03.016

Performance

Method Description
Psychosine is extracted from washed red blood cells and quantified using an isotopically labeled internal standard by liquid chromatography tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Tuesday, Thursday

Report Available
3 to 7 days

Specimen Retention Time
Residual whole blood: 14 days; Lysate: 2 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

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PSYR	Psychosine, RBC	93687-2

Result ID	Test Result Name	Result LOINC® Value
606152	Interpretation (PSYR)	59462-2
606145	Psychosine, RBC	93687-2
606151	Reviewed By	18771-6