MAYO CLINIC LABORATORIES

Test Definition: ARSAB

Arylsulfatase A, Blood Spot

Overview

Useful For

Second-tier newborn screening test for metachromatic leukodystrophy (MLD) when sulfatides are elevated

Enzymatic test for detection of arylsulfatase A deficiency

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

Genetics Test Information

Metachromatic leukodystrophy is caused by deficient activity of arylsulfatase A (ARSA) enzyme and is characterized by progressive neurologic changes and leukodystrophy with variable age of onset.

Pseudodeficiency of ARSA enzyme has been recognized among patients with other unrelated neurologic conditions as well as among the general population.

Additional studies, such as molecular genetic testing of *ARSA* (CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify *ARSA* Gene List ID: IEMCP-WHFH2K), urinary excretion of sulfatides (CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine), and, if necessary, histological analysis for metachromatic lipid deposits in nervous system tissue are recommended to confirm a diagnosis.

Testing Algorithm

For information see Newborn Screen Follow-up for Metachromatic Leukodystrophy

Special Instructions

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions
- Newborn Screen Follow-up For Metachromatic Leukodystrophy

Method Name

Flow Injection Analysis Tandem Mass Spectrometry (MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This test primarily serves as a second-tier assay to be used by newborn screening programs to screen for metachromatic leukodystrophy when first tier sulfatide analysis is abnormal. The test can also be used to screen patients at risk for metachromatic leukodystrophy.

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Card-Blood Spot Collection (Filter Paper)
Acceptable: PerkinElmer 226 filter paper, Munktell filter paper, Whatman protein Saver 903 paper, local newborn screening card, or blood collected in tubes containing EDTA (preferred) or heparin and dried on 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 filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry and freeze (with desiccant if necessary).
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

Biochemical Genetics Patient Information (T602)

Specimen Minimum Volume

1 Blood spot

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Nonapproved filter paper	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Frozen (preferred)	28 days	FILTER PAPER
	Refrigerated	14 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

Metachromatic leukodystrophy (MLD) is a lysosomal disorder caused by a deficiency of the enzyme arylsulfatase A (ARSA), which leads to the accumulation of sulfatides (both galactosyl and lactosyl sulfatide) in the white matter of the central nervous system, the peripheral nervous system, and, to a lesser extent, in visceral organs including the kidney and gallbladder. Cells that produce myelin are especially affected causing the characteristic leukodystrophy seen in MLD. Patients with MLD excrete excessive amounts of sulfatides in their urine.

The 3 clinical forms of MLD are late-infantile, juvenile, and adult, depending on age of onset. All forms result in progressive neurologic changes and leukodystrophy demonstrated on magnetic resonance imaging. To date, late-infantile MLD is most commonly diagnosed (50%-60% of cases) and usually presents before 30 months of age with hypotonia, clumsiness, diminished reflexes, and dysarthric speech. Progressive neurodegeneration occurs and, unless successfully treated, most patients do not survive past childhood. Juvenile MLD (20%-30% of cases) is characterized by onset between 30 months to 16 years old. Presenting features are behavior problems, declining school performance, clumsiness, and slurred speech. Neurodegeneration occurs at a somewhat slower and more variable rate than the late-infantile form. Adult MLD (15%-20% of cases) has an onset after puberty and can be as late as the fourth or fifth decade. Presenting features are often behavior and personality changes, including psychiatric symptoms. Clumsiness, neurologic symptoms, and seizures are also common. The disease course has variable progression and may occur over 2 to 3 decades.

Metachromatic leukodystrophy is an autosomal recessive disorder caused by disease-causing variants in the *ARSA* gene. This disorder is distinct from conditions caused by deficiencies of arylsulfatase B (Maroteaux-Lamy disease) and arylsulfatase C (steroid sulfatase deficiency). Saposin B deficiency is a rare autosomal recessive disorder with symptoms that mimic MLD; however, ARSA activity is not deficient. Like MLD, patients with saposin B deficiency can excrete excessive amounts of sulfatides in their urine. Individuals with multiple sulfatase deficiency, which is clinically distinct from MLD, will also have deficiency of ARSA, however, other sulfatase enzymes will also be deficient.

Individuals with "pseudodeficiency" of ARSA have very low levels of ARSA activity but are otherwise healthy. Pseudodeficiency has been found among patients with other unrelated neurologic conditions as well as among the general population, therefore a diagnosis of MLD cannot be based upon reduced ARSA activity alone. To confirm a diagnosis, additional studies, such as molecular genetic testing of *ARSA* (CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify Gene List ID: IEMCP-WHFH2K), urinary excretion of sulfatides (CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine), and/or histological analysis for metachromatic lipid deposits in nervous system tissue are recommended. While sulfatides appear to be elevated in newborn dried blood spots and is used as a primary newborn screening test, the utility of sulfatide analysis in dried blood spots outside of newborn screening has not been determined.

Current treatment options for MLD depend on the clinical stage and presence of neurologic symptoms. Allogenic hematopoietic stem cell transplant can treat symptoms related to the central nervous system in pre- and very early-symptomatic juvenile- or adult-onset MLD. Recently, autologous hematopoietic stem cell-based gene therapy has been approved in the U.S. and elsewhere for individuals with presymptomatic late-infantile MLD, presymptomatic juvenile MLD, or early-symptomatic juvenile MLD with maintained ability to walk and before the onset of cognitive decline.

Early diagnosis is extremely important to achieve optimal outcomes, especially for patients with late-infantile and early juvenile MLD. Therefore, newborn screening for MLD has been proposed and has recently been implemented in Norway, Austria, and parts of Germany. The approach entails measurement of sulfatides in the newborns dried blood spot followed by measurement of ARSA activity as a second-tier test when sulfatides are elevated. In the United States, New York is the first state to provide routine newborn screening for MLD.

Reference Values

Normal: > or =0.100 nmol/mL/hr

Interpretation

Reduced levels of arylsulfatase A (ARSA) are seen in patients with metachromatic leukodystrophy (MLD); however, some patients with MLD may have normal results by this method.

Individuals with pseudodeficiency of ARSA can have results in the affected range but are otherwise unaffected with MLD.

Reduced levels of ARSA are also possible when samples have been left at room temperature after drying.

Abnormal results and/or clinical suspicion should be confirmed using CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine and molecular genetic testing of *ARSA* (CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify Gene List ID: IEMCP-WHFH2K).

Cautions

This test is not reliable in identifying carriers.

Arylsulfatase A (ARSA) is also deficient in individuals with multiple sulfatase deficiency and possibly in saposin B deficiency.

Specimens not immediately refrigerated or frozen after drying may yield falsely low ARSA activity results.

This disorder is distinct from conditions caused by deficiencies of arylsulfatase B (Maroteaux-Lamy disease) and arylsulfatase C (steroid sulfatase deficiency).

Clinical Reference

1. Gomez-Ospina N. Arylsulfatase A deficiency. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1993-2025. Updated April 25, 2024. Accessed June 4, 2025. Available from: www.ncbi.nlm.nih.gov/books/NBK1130/
2. Fumagalli F, Calbi V, Natali Sora MG, et al. Lentiviral haematopoietic stem-cell gene therapy for early-onset metachromatic leukodystrophy: long-term results from a non-randomised, open-label, phase 1/2 trial and expanded access. Lancet. 2022;399(10322):372-383. doi:10.1016/S0140-6736(21)02017-1
3. Fumagalli F, Zambon AA, Rancoita PMV, et al. Metachromatic leukodystrophy: A single-center longitudinal study of 45 patients. J Inherit Metab Dis. 2021;44(5):1151-1164. doi:10.1002/jimd.12388
4. Laugwitz L, Mechtler TP, Janzen N, et al. Newborn screening and presymptomatic treatment of metachromatic leukodystrophy. N Engl J Med. 2024;391(13):1256-1258. doi:10.1056/NEJMc2407165

Performance

Method Description
A 3 mm sample is excised from a dried blood spot (DBS) specimen. Arylsulfatase A is isolated from the DBS aliquot by mixing with extraction reagent on a rotating incubator. The enzyme is then purified from the matrix using size exclusion chromatography. The sample is then incubated in the presence of internal standard, substrate, and assay buffer. Next, salts are removed using liquid/liquid extraction. A final purification step using solid phase extraction is performed before the dried down and reconstituted specimen is analyzed by flow injection tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday, Thursday

Report Available
3 to 6 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
82657

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ARSAB	Arylsulfatase A, BS	55912-0

Test Definition: ARSAB

Arylsulfatase A, Blood Spot

Result ID	Test Result Name	Result LOINC® Value
623015	Interpretation	59462-2
623013	Arylsulfatase A	55912-0
623014	Reviewed By	18771-6