MAYO CLINIC LABORATORIES

Test Definition: ARSAW

Arylsulfatase A, Leukocytes

Overview

Useful For

Preferred enzymatic test for detection of arylsulfatase A deficiency

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

Genetics Test Information

This is the preferred test to rule-out metachromatic leukodystrophy.

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

Pseudodeficiency of the ARSA enzyme has been recognized with increasing frequency among patients with other apparently 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), or histological analysis for metachromatic lipid deposits in nervous system tissue are recommended to confirm a diagnosis.

Testing Algorithm

For more information see the following:

-Lysosomal Disorders Diagnostic Algorithm, Part 2

-Newborn Screen Follow-up for Metachromatic Leukodystrophy

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Disorders Diagnostic Algorithm, Part 2
- Newborn Screen Follow-up For Metachromatic Leukodystrophy

Method Name

Colorimetric Enzyme Assay

NY State Available

Yes

Specimen

Specimen Type

Whole Blood ACD

Shipping Instructions

For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 6 days of collection to be stabilized. Pre-analytical processing is performed Monday through Friday and Sunday. This test may be canceled if specimens are outside of stability when processing occurs. Collect and package specimens for arrival on days when processing is performed.

Specimen Required

Container/Tube:
Preferred: Yellow top (ACD solution B)
Acceptable: Yellow top (ACD solution A)
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

5 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Metachromatic leukodystrophy (MLD) is a lysosomal storage 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. Late-infantile MLD is the most common (50%-60% of cases) and usually presents before 30 months of age with hypotonia, clumsiness, diminished reflexes, and slurred 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, the ARSA enzyme level is normal. 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 arylsulfatase A, 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), or, less commonly, histological analysis for metachromatic lipid deposits in nervous system tissue are recommended.

Current treatment options for MLD depend on the clinical stage and presence of neurologic symptoms. Early diagnosis is extremely important to improve clinical outcomes. Allogenic hematopoietic stem cell transplant (HSCT) 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 United States 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.

Reference Values

> or =62 nmol/h/mg

Note: Results from this assay may not reflect carrier status because of individual variation of arylsulfatase A enzyme levels. Low normal values may be due to the presence of pseudodeficiency or carrier alleles. Patients with these depressed levels may be phenotypically normal.

Interpretation

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

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

Abnormal results and/or clinical suspicion should be confirmed using CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine. If molecular confirmation is desired, consider 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.

Some patients with metachromatic leukodystrophy will not be detected by this method.

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

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

Clinical Reference

1. Gieselmann V, Ingeborg KM: Metachromatic leukodystrophy. In: Valle D, Antonarakis S, Ballabio A, Beaudet A, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed June 9, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546629
2. Gomez-Ospina N. Arylsulfatase A deficiency. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews[Internet]. University of Washington, Seattle; 2006.Updated April 25,2024. Accessed June 9, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1130/
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

p-Nitrocatechol sulfate (2-hydroxy-5-nitrophenyl sulfate) is used as an analog to the natural substrate. The reaction yields *p*-nitrocatechol, which is measured at 515 nm.(Shapira E, Blitzer MG, Africk DK, et al: Enzyme assays: arylsulfatase A activity. In: Biochemical Genetics: A Laboratory Manual. Oxford University Press; 1989:41-42; Cowan T, Pasquali M: Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KD, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

PDF Report

No

Day(s) Performed

Preanalytical processing: Monday through Friday, Sunday

Assay performed: Wednesday

Report Available
2 to 8 days

Specimen Retention Time
WBC 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

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ARSAW	Arylsulfatase A, Leukocytes	24078-8

Result ID	Test Result Name	Result LOINC® Value
8779	Arylsulfatase A, Leukocytes	24078-8
32437	Interpretation	59462-2
32438	Reason for referral	42349-1
32439	Reviewed by	18771-6