MAYO CLINIC LABORATORIES

Test Definition: ARSU

Arylsulfatase A, 24 Hour, Urine

Overview

Useful For

Detection of arylsulfatase A deficiency using urine specimens

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

Genetics Test Information

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.

This test is not suitable for carrier detection.

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 information see Lysosomal Disorders Diagnostic Algorithm, Part 2

Special Instructions

- Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens
- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Disorders Diagnostic Algorithm, Part 2

Method Name

Colorimetric, Enzyme Assay

NY State Available

Yes

Specimen

Specimen Type

Urine

Ordering Guidance

Leukocytes are the preferred screening specimen for metachromatic leukodystrophy. The preferred test to rule-out metachromatic leukodystrophy is ARSAW / Arylsulfatase A, Leukocytes.

Shipping Instructions

Specimen must be received at least 1 day prior to assay day for processing.

Necessary Information

24-Hour volume (in milliliters) is required.

Specimen Required

Supplies: Urine Tubes, 10 mL (T068)
Container/Tube: Plastic, 10-mL tube
Specimen Volume: 6 mL
Collection Instructions:
1. Collect a 24-hour urine specimen.
2. No added preservative.
3. Refrigerate specimen during collection.
Additional Information: For multiple collections see Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens.

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.

Urine Preservative Collection Options

Note: The application of temperature controls **must occur during** collection.

Ambient (no additive)	No
Refrigerate (no additive)	Required
Frozen (no additive)	No
50% Acetic Acid	No
Boric Acid	No
Diazolidinyl Urea	No
6M Hydrochloric Acid	No
6M Nitric Acid	No
Sodium Carbonate	No
Toluene	No

Specimen Minimum Volume

2.5 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
Urine	Refrigerated	14 days	

Clinical & Interpretive

Clinical Information

Metachromatic leukodystrophy (MLD) is a lysosomal storage disorder caused by a deficiency of the arylsulfatase A (ARSA) enzyme, 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. 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 also 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 =19 nmol/h/mL

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).

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

Abnormal results 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

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

This test is not reliable in identifying carriers due both to analytical variation and unusual genetic variants.

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

Dialyzed urine is mixed with the artificial substrate *p*-nitrocatechol sulfate. As sulfate is released, the freed *p*-nitrocatechol is measured in alkaline solution at 515 nm.(Baum H, Dodgson KS, Spencer B: The assay of arylsulfatases A and B in human urine. Clin Chim Acta 1959;4[3]:453-455; 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

Tuesday

Report Available

3 to 9 days

Specimen Retention Time

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

84311

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ARSU	Arylsulfatase A, U	42726-0

Result ID	Test Result Name	Result LOINC® Value
8777	Arylsulfatase A, U	42726-0
37423	Interpretation (ARSU)	59462-2
37413	Reviewed By	18771-6