Test Definition: CTSU

Ceramide Trihexosides and Sulfatides, Random, Urine

Overview

Useful For

Identifying patients with Fabry disease

Identifying patients with metachromatic leukodystrophy

Identifying patients with saposin B deficiency

Identifying patients with multiple sulfatase deficiency

Identifying patients with mucolipidosis II (I-cell disease)

Genetics Test Information

Many patients with Fabry disease excrete ceramide trihexosides in their urine. Patients with either metachromatic leukodystrophy or multiple sulfatase deficiency excrete sulfatides. While patients with saposin B deficiency and some patients with mucolipidosis II (I-cell disease) excrete both ceramide trihexosides and sulfatides.

Specific enzyme or molecular analysis should be performed to confirm a positive test result.

Testing Algorithm

For information see:
-Fabry Disease Diagnostic Testing Algorithm
-Lysosomal Disorders Screen Interpretive Algorithm
-Newborn Screen Follow-up for Metachromatic Leukodystrophy

If the patient has abnormal newborn screening results for Fabry disease. Refer to the appropriate ACMG Newborn Screening ACT Sheet.(1)

Special Instructions

- Fabry Disease Diagnostic Testing Algorithm
- Biochemical Genetics Patient Information
- Lysosomal Disorders Diagnostic Algorithm, Part 2
- Lysosomal Disorders Screen Interpretive Algorithm
- Newborn Screen Follow-up For Metachromatic Leukodystrophy

Method Name

Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)

NY State Available

Yes

Specimen

Specimen Type
Urine

Necessary Information
Biochemical Genetics Patient Information (T602) is recommended. This information aids in providing a more thorough interpretation of results. Send information with specimen.

Specimen Required
Patient Preparation: Prior to urine collection, patient **should not** use baby wipes or wipes containing soaps as these may interfere with testing.
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Container/Tube: Plastic, 5-mL urine tube
Specimen Volume: 2 mL
Collection Instructions: Collect a **first-morning**, random urine specimen.
Specimen Stability Information: Refrigerated (preferred) 45 days/Ambient 45 days/Frozen 19 months

Forms
1. Biochemical Genetics Patient Information (T602)
2. 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
Urine	Refrigerated (preferred)	45 days	
	Ambient	45 days	
	Frozen		

Clinical & Interpretive

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

Urinary excretion of ceramide trihexosides (CT) can be suggestive of Fabry disease, while excretion of sulfatide with or without CT can be suggestive of metachromatic leukodystrophy, multiple sulfatase deficiency, mucolipidosis II (I-cell disease), or saposin B deficiency.

Fabry disease is an X-linked lysosomal storage disorder caused by a deficiency of the enzyme alpha-galactosidase A (alpha-Gal A). Affected individuals accumulate glycosphingolipids in the lysosomes throughout the body, particularly in the kidney, heart, and brain. Severity and onset of symptoms are dependent on the amount of residual enzyme activity. Symptoms may include acroparesthesias (pain crises), multiple angiokeratomas, reduced or absent sweating, corneal opacity, renal insufficiency leading to kidney failure, and cardiac and cerebrovascular disease. There are renal and cardiac variant forms of Fabry disease that may be underdiagnosed. Females with Fabry disease can have clinical presentations ranging from asymptomatic to severely affected, and they may have alpha-Gal A activity in the normal range. Regardless of the severity of symptoms, individuals with Fabry disease may show an increased excretion of CT in urine.

Metachromatic leukodystrophy (MLD) is an autosomal recessive lysosomal storage disorder most frequently caused by a deficiency of the arylsulfatase A enzyme. Various sulfatides accumulate in the brain, nervous system, and visceral organs, including the kidney and gallbladder and are excreted in the urine. Based on age of onset, the 3 clinical forms of MLD are late-infantile, juvenile, and adult, with late-infantile being the most common. All result in progressive neurologic changes and leukodystrophy demonstrated on magnetic resonance imaging. Symptoms may include hypotonia, clumsiness, diminished reflexes, slurred speech, behavioral problems, and personality changes. Individuals with MLD show an increased urinary excretion of sulfatides without CT.

Saposin B deficiency is a rare condition with clinical features that mimic MLD; however, individuals with saposin B deficiency have normal arylsulfatase A activity. Individuals with saposin B deficiency typically have an increased urinary excretion of both sulfatides and CT.

Low arylsulfatase A activity has been found in some clinically normal parents and other relatives of MLD patients. Individuals with this "pseudodeficiency" have been recognized with increasing frequency among patients with other apparently unrelated neurologic conditions as well as among the general population. This has been associated with a fairly common variant in the arylsulfatase A gene (*ARSA*), which leads to low expression of the enzyme (5%-20% of normal). These individuals do not have metachromatic deposits in peripheral nerve tissues, and their urine sulfatides content is normal.

Multiple sulfatase deficiency (MSD) is a rare autosomal recessive disorder caused by disease-causing variants in *SUMF1,* which is required for post-translational activation of the family of 17 sulfatase enzymes, including arylsulfatase A and B. The clinical features of MSD include those of late-infantile MLD, dysmorphic features similar to the mucopolysaccharidoses, and ichthyosis as seen in steroid sulfatase deficiency. Individuals with MSD typically have an increased urinary excretion of sulfatides as well as increased urinary glycosaminoglycans (MPSQU / Mucopolysaccharides Quantitative, Random, Urine).

Mucolipidosis II, also known as I-cell disease, is a rare autosomal recessive disorder with features of both mucopolysaccharidoses and sphingolipidoses. I-cell disease is a progressive disorder characterized by congenital or early infantile manifestations including coarse facial features, short stature, skeletal anomalies, cardio- and hepatomegaly, and developmental delays. Individuals with I-cell disease have abnormal oligosaccharide profiles (OLIGU /

Oligosaccharide Screen, Random, Urine) and may show an increased urinary excretion of both CT and sulfatides.

Reference Values
An interpretive report will be provided.

Interpretation
The pattern of ceramide trihexosides or sulfatide excretion will be described. A normal pattern of excretion suggests absence of these diseases (see Cautions).

Evidence of ceramide trihexoside accumulation suggests decreased or deficient alpha-galactosidase activity, see Fabry Disease Diagnostic Testing Algorithm.

Evidence of sulfatide accumulation suggests decreased or deficient arylsulfatase A activity. Follow-up with the specific enzyme assay is recommended:
-ARSAW / Arylsulfatase A, Leukocytes (preferred)
-ARSU / Arylsulfatase A, 24 Hour, Urine

To exclude multiple sulfatase deficiency (MSD), determination of iduronate-2-sulfatase activity is recommended.
-I2SWB / Iduronate-2-Sulfatase, Leukocytes
-I2SB / Iduronate-2-Sulfatase, Blood Spot

Evidence of both ceramide trihexoside and sulfatide accumulation suggests a diagnosis of mucolipidosis II (I-cell disease) or saposin B deficiency. Follow-up testing to rule-out I-cell disease may include molecular analysis of the *GNPTAB* gene or measurement of serum hydrolases (NAGS / Hexosaminidase A and Total Hexosaminidase, Serum).

Molecular genetic testing is required to confirm saposin B deficiency.

For more information see Lysosomal Disorders Diagnostic Algorithm, Part 2 and Lysosomal Disorders Screen Interpretive Algorithm.

Cautions
Specific enzymatic or molecular assays should be used to confirm positive results.

In some instances, normal excretion of ceramide trihexosides may be seen in individuals affected with Fabry disease. If Fabry disease is clinically suspected, see Fabry Disease Diagnostic Testing Algorithm for additional testing recommendations.

Clinical Reference
1. Pino G, Conboy E, Tortorelli S, et al. Multiplex testing for the screening of lysosomal storage disease in urine: Sulfatides and glycosaminoglycan profiles in 40 cases of sulfatiduria. Mol Genet Metab. 2020;129(2):106-110. doi:10.1016/j.ymgme.2019.10.009
2. ACMG Newborn Screening ACT Sheets. Accessed May 12, 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
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A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw Hill; 2019. Accessed May 12, 2025. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225546984
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5. Mehta A, Hughes DA. Fabry disease. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2002. Updated April 11, 2024. Accessed May 12, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1292/
6. Schlotawa L, Ennemann EC, Radhakrishnan K, et al. SUMF1 mutations affecting stability and activity of formylglycine generating enzyme predict clinical outcome in multiple sulfatase deficiency. Eur J Hum Genet. 2011;19(3):253-261
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8. Leroy JG, Cathey SS, Friez MJ. GNPTAB-related disorders. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2008. Updated August 29, 2019. Accessed May 12, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1828/

Performance

Method Description
Ceramide trihexosides and sulfatides are determined by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis. Urine specimens are centrifuged and all but 50 mcL of supernatant is discarded from the pellet. Methanol including internal standards is added, and then ceramide trihexosides and sulfatides are extracted in chloroform. After centrifugation, the bottom chloroform layer is spotted onto a MALDI plate, matrix is added and allowed to air dry. The plate is then analyzed using a MALDI TOF/TOF 5800 Analyzer.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Tuesday

Report Available
2 to 8 days

Specimen Retention Time
1 month

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Test Definition: CTSU

Ceramide Trihexosides and Sulfatides, Random, Urine

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

83789

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CTSU	Ceramide Trihex and Sulfatide, U	59462-2

Result ID	Test Result Name	Result LOINC® Value
606148	Interpretation	59462-2
606149	Reviewed By	18771-6