

## Overview

### Useful For

Evaluation of patients with a clinical presentation suggestive of lysosomal acid lipase deficiency using blood spot specimens

This test is **not useful** to determine carrier status for cholesteryl ester storage disease or Wolman disease.

### Genetics Test Information

This test provides diagnostic testing for patients with clinical signs and symptoms suspicious for lysosomal acid lipase deficiency (LALD).

LALD is expressed phenotypically as infantile-onset Wolman disease or later-onset cholesterol ester storage disease.

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Biochemical Genetics Patient Information](#)
- [Blood Spot Collection Card-Spanish Instructions](#)
- [Blood Spot Collection Card-Chinese Instructions](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Blood Spot Collection Instructions](#)

### Method Name

Fluorometric Enzyme Assay

### NY State Available

Yes

## Specimen

### Specimen Type

Whole blood

### Necessary Information

Provide a reason for testing with each specimen.

### Specimen Required

**Supplies:** Card-Blood Spot Collection (Filter Paper) (T493)

**Collection Container/Tube:**

**Preferred:** Blood spot collection card

**Acceptable:** PerkinElmer 226 filter paper, Munktell TFN, and Whatman Protein Saver 903 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. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see [How to Collect Dried Blood Spot Samples](#).
3. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. Keep specimen dry.

**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**

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 1 of the following forms with the specimen:
  - [Biochemical Genetics Test Request](#) (T798)
  - [Gastroenterology and Hepatology Test Request](#) (T728)

**Specimen Minimum Volume**

1 Blood spot

**Reject Due To**

|                                      |        |
|--------------------------------------|--------|
| Shows serum rings<br>Multiple layers | Reject |
|--------------------------------------|--------|

**Specimen Stability Information**

| Specimen Type | Temperature              | Time    | Special Container |
|---------------|--------------------------|---------|-------------------|
| Whole blood   | Refrigerated (preferred) | 28 days | FILTER PAPER      |
|               | Ambient                  | 7 days  | FILTER PAPER      |
|               | Frozen                   | 90 days | FILTER PAPER      |

**Clinical & Interpretive****Clinical Information**

Deficiency of lysosomal acid lipase (LAL) results in 2 clinically distinct phenotypes, Wolman disease (WD) and cholesteryl ester storage disease (CESD). Both phenotypes follow an autosomal recessive inheritance pattern and are caused by

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variant in the *LIPA* gene.

WD, the early-onset phenotype of LAL deficiency, is a lipid storage disorder characterized by vomiting, diarrhea, failure to thrive, abdominal distension, hepatosplenomegaly, and liver failure. Enlarged adrenal glands with calcification, a classic finding in WD, can lead to adrenal cortical insufficiency. Unless successfully treated, survival is rare beyond infancy.

CESD, the late-onset phenotype of LAL deficiency, is clinically variable with patients presenting at any age with progressive hepatomegaly and often splenomegaly, serum lipid abnormalities, and elevated liver enzymes. In childhood, patients can also present with failure to thrive and delayed milestones. Common features include premature atherosclerosis leading to coronary artery disease and strokes, liver disease of varying severity, and organomegaly. Lipid deposition in the intestinal tract can lead to diarrhea and weight loss.

CESD is likely underdiagnosed and frequently diagnosed incidentally after liver pathology reveals findings similar to nonalcoholic fatty liver disease or nonalcoholic steatohepatitis. Birefringent cholesteryl ester crystals in hepatocytes or Kupffer cells in fresh-frozen tissues are visualized under polarized light and pathognomonic.

Enzyme replacement therapy (sebelipase alfa) was recently approved for both WD and CESD and is now clinically available.

### Reference Values

> or =21.0 nmol/h/mL

### Interpretation

Enzyme activity below 1.5 nmol/h/mL in properly submitted samples is consistent with lysosomal acid lipase deficiency: Wolman disease or cholesteryl ester storage disease.

Normal results (> or =21.0 nmol/h/mL) are not consistent with lysosomal acid lipase deficiency.

### Cautions

No significant cautionary statements

### Clinical Reference

1. Bernstein DL, Hulkova H, Bialer MG, Desnick RJ. Cholesteryl ester storage disease: review of the findings in 135 reported patients with an underdiagnosed disease. *J Hepatol.* 2013;58(6):1230-1243
2. Reynolds T. Cholesteryl ester storage disease: a rare and possibly treatable cause of premature vascular disease and cirrhosis. *J Clin Pathol.* 2013;66(11):918-923
3. Pericleous M, Kelly C, Wang T, Livingstone C, Ala A. Wolman's disease and cholesteryl ester storage disorder: the phenotypic spectrum of lysosomal acid lipase deficiency. *Lancet Gastroenterol Hepatol.* 2017;2(9):670-679. doi:10.1016/S2468-1253(17)30052-3
4. Pastores GM, Hughes DA. Lysosomal acid lipase deficiency: Therapeutic options. *Drug Des Devel Ther.* 2020;14:591-601

### Performance

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**Method Description**

A 3-mm (one-eighth inch) disk is punched out of the dried blood spot into a microcentrifuge tube and water is added as a preincubation extraction that takes place on an orbital shaker. Extraction liquid is combined with either water (total activity well) or Lalistat (inhibited well) in a black 96-well plate. The plate is incubated. The substrate is then added to the same plate. After the incubation period, calibrators are prepared and analyzed on every plate to calculate enzyme activity results based on fluorescence units in patient wells vs calibrators. The calibration is derived from 4-methylumbelliferone (4-MU) that is serially diluted manually in the plate, with the highest calibrator being equivalent to an enzyme activity of 672.0 nmol/hour/mL blood. The plate is then ready to be read using the spectrofluorometer. Enzyme activity is calculated by subtracting the inhibited activity from total activity. (Hamilton J, Jones I, Srivastava R, Galloway P. A new method for the measurement of lysosomal acid lipase in dried blood spots using the inhibitor Lalistat 2. Clin Chim Acta. 2012;413(15-16):1207-1210; Cowan T, Pasquali M: Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

**PDF Report**

No

**Day(s) Performed**

Thursday

**Report Available**

2 to 8 days

**Specimen Retention Time**

1 year

**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 |
|---------|---------------------------|--------------------|
| LALBS   | Lysosomal Acid Lipase, BS | 73958-1            |

| Result ID | Test Result Name          | Result LOINC® Value |
|-----------|---------------------------|---------------------|
| 62955     | Lysosomal Acid Lipase, BS | 73958-1             |
| 36341     | Reviewed By               | 18771-6             |
| 36340     | Interpretation (LALBS)    | 59462-2             |