

Overview

Useful For

Second-tier newborn screen for tyrosinemia type 1 (HT-1) when primary screen showed nonspecific elevations of tyrosine

Diagnosing HT-1 when used in conjunction with testing for urine organic acids, liver function, alpha-fetoprotein, and molecular genetic analysis of *FAH*

Genetics Test Information

This test is a second-tier newborn screen for tyrosinemia type 1.

Special Instructions

- [Blood Spot Collection Card-Spanish Instructions](#)
- [Blood Spot Collection Card-Chinese Instructions](#)
- [Blood Spot Collection Instructions](#)

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

The preferred test for diagnosis and monitoring of patients with tyrosinemia type 1 is TYRBS / Tyrosinemia Follow Up Panel, Blood Spot.

Necessary Information

Patient's age is required.

Specimen Required

Submit only 1 of the following specimen types:

Preferred:

Specimen Type: Blood Spot

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

Container/Tube:**Preferred:** Blood Spot Collection Card**Acceptable:** Whatman Protein Saver 903 Paper, PerkinElmer 226 filter paper, Munktell filter paper, or blood collected in tube containing EDTA and dried on filter paper.**Specimen Volume:** 2 blood spots**Collection Instructions:**

1. At least 1 spot should be complete (ie, unpunched).
2. Do not expose specimen to heat or direct sunlight.
3. Do not stack wet specimens.
4. Keep specimen dry.
5. If collection of a new specimen is necessary, let blood dry on the Blood Spot Collection Card (T493) at ambient temperature in a horizontal position for a minimum of 3 hours.

Specimen Stability Information: Ambient (preferred) 7 days/Refrigerated 14 days/Frozen 90 days**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)

Acceptable**Specimen Type:** Whole Blood**Container/Tube:** Lavender top (EDTA)**Specimen Volume:** 2 mL**Collection Instructions:** Send whole blood specimen in original tube. **Do not aliquot.****Specimen Stability Information:** Refrigerate 6 days**Forms**[If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request](#) (T798) with the specimen.**Specimen Minimum Volume**

Blood Spot: 1

Whole Blood: 0.5 mL

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Unapproved filter papers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Varies		

Clinical & Interpretive

Clinical Information

Tyrosinemia type 1 (hepatorenal tyrosinemia, HT-1) is an autosomal recessive condition caused by a deficiency of the enzyme fumarylacetoacetate hydrolase (FAH). HT-1 primarily affects the liver, kidneys, and peripheral nerves, causing severe liver disease, renal tubular dysfunction, and neurologic crises. If left untreated, most patients die of liver failure in the first years of life and all are at risk of developing hepatocellular carcinoma. Treatment with 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3 cyclohexanedione (NTBC) is available and is particularly effective when initiated in newborns. The incidence of HT-1 is approximately 1 in 100,000 live births.

While tyrosine can be determined by routine newborn screening, it is not a specific marker for tyrosinemia type I and often may be associated with common and benign transient tyrosinemia of the newborn. Succinylacetone is a specific marker for HT-1 but not consistently measured by newborn screening programs. This assay determines succinylacetone and tyrosine in newborn blood spots by tandem mass spectrometry. Additional follow-up testing may include confirmatory molecular analysis of the *FAH* gene.

Reference Values

SUCCINYLACETONE

< or =1.0 nmol/mL

TYROSINE

<4 weeks: 40-280 nmol/mL

> or =4 weeks: 25-150 nmol/mL

Interpretation

Elevations of succinylacetone (SUAC) above the reference range with or without elevations of tyrosine (TYR) are indicative of tyrosinemia type 1.

Elevations of TYR above the reference range without elevations of SUAC may be suggestive of tyrosinemia type II, type III, transient hypertyrosinemia of the neonate, or nonspecific liver disease.

Cautions

Normal levels may be seen in affected individuals undergoing treatment.

In rare cases of tyrosinemia type 1, tyrosine or succinylacetone may not be elevated.(1)

Clinical Reference

- Blackburn PR, Hickey RD, Nace RA, et al. Silent tyrosinemia type I without elevated tyrosine or succinylacetone associated with liver cirrhosis and hepatocellular carcinoma. *Hum Mutat.* 2016;37(10):1097-1105. doi:10.1002/humu.23047
- Larochelle J, Alvarez F, Bussieres JF, et al. Effects of nitisinone (NTBC) treatment on the clinical course of hepatorenal tyrosinemia in Quebec. *Mol Genet Metab.* 2012;107(1-2):49-54

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3. Sniderman King L, Trahms C, Scott CR. Tyrosinemia Type I. In: MP Adam, HH Ardinger, PA Pagon et al, eds: GeneReviews [Internet]. University of Washington, Seattle; 2006. Updated May 25, 2017. Accessed December 7, 2023. Available at: www.ncbi.nlm.nih.gov/books/NBK1515/
 4. De Jesus VR, Adam BW, Mandel D, Cuthbert CD, Matern D. Succinylacetone as primary marker to detect tyrosinemia type I in newborns and its measurement by newborn screening programs. *Mol Genet Metab.* 2014;113(1-2):67-75
 5. Chinsky JM, Singh R, Ficicioglu C et al. Diagnosis and treatment of tyrosinemia type I: a US and Canadian consensus group review and recommendations. *Genet Med.* 2017;19(12) doi:10.1038/gim.2017.101

Performance

Method Description

A 3-mm disk is punched out of the dried blood spot onto a 96-well plate. The amino acids are extracted by the addition of acetonitrile and a known concentration of isotopically labeled amino acids as internal standards. The extract is moved to another 96-well plate, dried under a stream of nitrogen, and derivatized by the addition of n-butanol hydrochloric acid. Analytes are measured by liquid chromatography tandem mass spectrometry. The concentrations of the analytes are established by computerized comparison of ion intensities of these analytes to that of the respective internal standards.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

3 to 5 days

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

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

84510

82542

82542 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SUAC	Succinylacetone, BS	53231-7

Result ID	Test Result Name	Result LOINC® Value
22714	Interpretation	59462-2
22716	Reviewed By	18771-6
607629	Succinylacetone	53231-7
607630	Tyrosine	35571-9