Test Definition: TYRBS

Tyrosinemia Follow Up Panel, Blood Spot

Overview

Useful For

Monitoring of individuals with tyrosinemia type 1 (HT-1)

Diagnosis of HT-1 when used in conjunction with testing for urine organic acids, liver function, alpha-fetoprotein, and molecular genetic analysis of the fumarylacetoacetate hydrolase (*FAH)* gene

Genetics Test Information

This test assists in the diagnosis of tyrosinemia type 1 (HT-1) and monitoring of the effectiveness of 2-[2-nitro-4-trifluoromethylbenzoyl]-1,3-cycohexanedione (NTBC; nitisinone) and dietary therapy in patients with HT-1.

Testing Algorithm

For information see Newborn Screen Follow-up for Elevated/Normal Tyrosine, Elevated Succinylacetone

Special Instructions

- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions
- Newborn Screen Follow-up for Elevated/Normal Tyrosine, Elevated Succinylacetone

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Necessary Information

Patient's age and reason for testing are 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 tubes containing EDTA and dried on filter paper
Specimen Volume: 2 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. At least 2 spots should be complete (ie, unpunched).
3. Let blood dry on filter paper at room 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.
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:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 2 mL
Collection Instructions:
1. Invert several times to mix blood.
2. 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 spots: 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. 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 (HCC). The incidence of HT-1 is approximately 1 in 100,000 live births.

Affected individuals can show a partial response to dietary restriction of phenylalanine and tyrosine, but dietary treatment in conjunction with the administration of 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3 cyclohexanedione (NTBC; nitisinone), an inhibitor of the proximal tyrosinemia pathway, is very effective when initiated in newborns. Outcome data are promising, and to date, newborn patients treated with NTBC have not developed acute liver disease, neurologic crises, or HCC.

According to treatment guidelines established in 2017, monitoring of blood NTBC concentration and succinylacetone (SUAC) levels along with measuring the dietary intake of amino acids, including tyrosine and phenylalanine are part of an individualized surveillance plan for patients with HT-1.(1) Monthly analysis of SUAC, NTBC concentration, and amino acids is suggested for the first year of life with the same compounds being monitored every 3 months until age 5 and every 6 months thereafter.

The analytes encompassed in this assay satisfy the recommendations for diagnosis and monitoring of HT-1. In particular, for NTBC, the current guidelines recommend 40 nmol/mL to 60 nmol/mL plasma concentration, which corresponds to a target range for NTBC in dried blood spots of 17 nmol/mL to 26 nmol/mL based on a blood to plasma conversion factor of 2.34.(2)

Reference Values

Tyrosine:
<4 weeks 40-280 nmol/mL
> or =4 weeks 25-150 nmol/mL

Phenylalanine: 27-107 nmol/mL

Methionine: 11-45 nmol/mL

Succinylacetone: < or =1.0 nmol/mL

Nitisinone: < or =0.5 nmol/mL

Interpretation

Quantitative results with reference values are reported without added interpretation. When applicable, reports of abnormal results may contain an interpretation based on available clinical information.

Cautions

Bornaprine (Sormodrem) may, at least in theory, interfere with accurate measurement of 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3 cyclohexanedione (NTBC, nitisinone).

In rare cases of tyrosinemia type 1, tyrosine or succinylacetone may not be elevated.(3)

Clinical Reference

1. Chinsky JM, Singh R, Ficiciolglu 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
2. Laeremans H, Turner C, Andersson T, et al. Inter-laboratory analytical improvement of succinylacetone and nitisinone quantification from dried blood spot samples. JIMD Rep. 2020;53(1):90-102
3. 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
4. Ficicioglu C. Tyrosinemia Type I. In: Adam MP, Feldman J, Mirzaa GM, et al, eds: GeneReviews [Internet]. University of Washington, Seattle; 2006. Updated November 20, 2025. Accessed December 30, 2025. Available at: www.ncbi.nlm.nih.gov/books/NBK1515/

Performance

Method Description

A 3-mm disk is punched out of the dried blood spot into a 96-well plate. The amino acids and nitisinone are extracted by the addition of acetonitrile and known concentrations 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

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

84510
84030
82542
80299
82131
82542 only (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TYRBS	Tyrosinemia Follow Up Panel, BS	94573-3

Result ID	Test Result Name	Result LOINC® Value
607553	Tyrosine	35571-9
607554	Phenylalanine	29573-3
607555	Methionine	47700-0
607556	Succinylacetone	53231-7
607557	Nitisinone	85098-2
607552	Reviewed By	18771-6
BG722	Reason for Referral	42349-1