MAYO CLINIC LABORATORIES

Test Definition: PKU

Phenylalanine and Tyrosine, Plasma

Overview

Useful For

Monitoring effectiveness of dietary therapy in patients with hyperphenylalaninemia

Genetics Test Information

Defects in phenylalanine hydroxylase (PAH) cause the majority of cases of hyperphenylalaninemia (HPA); however, approximately 2% of infants with HPA have impaired synthesis or recycling of tetrahydrobiopterin (BH4).

Phenylketonuria: Evaluation of patients with hyperphenylalaninemia or monitoring effectiveness of dietary therapy. This test is not sufficient follow-up for abnormal newborn screening results, because other causes of HPA (eg, BH4 deficiency) cannot be excluded by this test alone.

Tyrosinemia, type I**:** For medical management

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Plasma

Necessary Information

1. Patient's age is required.

2. Include family history, clinical condition (asymptomatic or acute episode), diet, and drug therapy information.

Specimen Required

Patient Preparation:

Fasting: 8 hours, required; Infants should have specimen collected before next feeding

Collection Container/Tube:

Preferred: Green top (sodium heparin)

Acceptable: Green top (lithium heparin), lavender top (EDTA)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Collection Instructions:

1. Centrifuge and aliquot plasma into a plastic vial.
2. Send plasma frozen.

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

0.1 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Frozen (preferred)	14 days	
	Refrigerated	14 days	

Clinical & Interpretive

Clinical Information

Phenylketonuria (PKU) is the most frequent inherited disorder of amino acid metabolism (about 1:10,000-1:15,000) and was the first successfully treated inborn error of metabolism. It is inherited in an autosomal recessive manner and is caused by a defect in the enzyme phenylalanine hydroxylase (PAH), which converts the essential amino acid phenylalanine to tyrosine. Deficiency of PAH results in decreased levels of tyrosine and an accumulation of phenylalanine in blood and tissues. If left untreated, PKU leads to severe brain damage with intellectual impairment, behavior abnormalities, seizures, and spasticity. The level of enzyme activity differentiates classic PKU (PAH activity <1%) from other milder forms; however, all are characterized by increased levels of phenylalanine (hyperphenylalaninemia). Treatment includes the early introduction of a diet low in phenylalanine.

Tetrahydrobiopterin (BH4) is a cofactor of PAH as well as tyrosine and tryptophan hydroxylase. Approximately 2% of patients with hyperphenylalaninemia have a deficiency of BH4, which causes a secondary deficit of the neurotransmitters, dopamine and serotonin. There are 4 autosomal recessive disorders associated with BH4 deficiency plus hyperphenylalaninemia: guanosine triphosphate cyclohydrolase deficiency; 6-pyruvoyl tetrahydropterin synthase deficiency; dihydropteridine reductase deficiency; and pterin-4 alpha carbinolamine dehydratase (PCD) deficiency. This group of disorders, with the exception of PCD, is characterized by progressive dystonia, truncal hypotonia, extremity hypertonia, seizures, and intellectual disability though milder presentations exist. PCD has no symptoms other than transient alterations in tone. Treatment may include administration of BH4, L-dopa (and carbidopa) 5-hydroxytryptophan supplements, and a low phenylalanine diet.

Tyrosine is a nonessential amino acid, which is derived from dietary sources, the hydroxylation of phenylalanine, or protein breakdown. Primary PKU and secondary (defects of BH4 metabolism) hyperphenylalaninemia can cause abnormally low levels of tyrosine. Measurement of the phenylalanine:tyrosine ratio is helpful in monitoring appropriate

dietary intake.

Reference Values

PHENYLALANINE
Premature: 98-213 nmol/mL
0-31 days: 38-137 nmol/mL
1-24 months: 31-75 nmol/mL
2-18 years: 26-91 nmol/mL
> or =19 years: 35-85 nmol/mL

Conversion Formulas:
Result in mg/dL x 60.5=result in nmol/mL
Result in nmol/mL x 0.0165=result in mg/dL

TYROSINE
Premature: 147-420 nmol/mL
0-31 days: 55-147 nmol/mL
1-24 months: 22-108 nmol/mL
2-18 years: 24-115 nmol/mL
> or =19 years: 34-112 nmol/mL

Conversion Formulas:
Result in mg/dL x 55.2=result in nmol/mL
Result in nmol/mL x 0.0181=result in mg/dL

Interpretation

The quantitative results of phenylalanine and tyrosine with age-dependent reference values are reported without added interpretation. When applicable, reports of abnormal results may contain an interpretation based on available clinical interpretation.

A phenylalanine:tyrosine ratio higher than 3 is considered abnormal.

Cautions

This test is not sufficient to establish a diagnosis of hyperphenylalaninemia.

Clinical Reference

1. Mitchell GA, Grompe M, Lambert M, Tanguay RM. Hypertyrosinemia. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw Hill; 2019. Accessed October 2, 2024. Available at https://ommbid.mhmedical.com/content.aspx? bookid=2709&sectionid=225082825
2. Donlon J, Sarkissian C, Levy H, Scriver CR. Hyperphenylalaninemia: Phenylalanine hydroxylase deficiency. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed October 2, 2024. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225081923
3. Burgard P, Luo X, Hoffmann GF. Phenylketonuria. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. McGraw-Hill Medical Division; 2009:163-168
4. Blau N, Thony B. Hyperphenylalanemias: Disorders of tetrahydrobiopterin metabolism. In: Sarafoglou K, Hoffmann GF,

Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. McGraw-Hill Medical Division; 2009:169-175

Performance

Method Description

This method quantifies phenylalanine (Phe) and tyrosine (Tyr) using stable isotope-labeled internal standards (IS): d5-Phe and d4-Tyr. Phe and Tyr are extracted from plasma. The supernatant is diluted and then introduced into the tandem mass spectrometer. The concentration of Phe and Tyr are established by comparison of the ion intensity with that of the IS.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

2 to 4 days

Specimen Retention Time

2 weeks

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

84030 Phenylalanine
84510 Tyrosine
82542 (if appropriate for government payers)

LOINC® Information

MAYO CLINIC LABORATORIES

Test Definition: PKU

Phenylalanine and Tyrosine, Plasma

Test ID	Test Order Name	Order LOINC® Value
PKU	Phenylalanine and Tyrosine, P	101402-6

Result ID	Test Result Name	Result LOINC® Value
8380	Phenylalanine, P	14875-9
8627	Tyrosine, P	20660-7