Overview

Useful For
Monitoring effectiveness of dietary therapy in patients with hyperphenylalaninemia

Genetics Test Information

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 hyperphenylalaninemia (eg, BH4 deficiency) cannot be excluded by this test alone.

Tyrosinemia, type I: For medical management.

Highlights
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).

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 (4 hours or more in infants)

Collection Container/Tube:
Preferred: Green top (sodium heparin)
Acceptable: Lavender top (EDTA)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Forms
If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.
Specimen Minimum Volume
0.1 mL

Reject Due To

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<tr>
<td>Gross lipemia</td>
<td>OK</td>
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<tr>
<td>Gross icterus</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
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<th>Time</th>
<th>Special Container</th>
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<tr>
<td></td>
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Clinical and 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. 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 not only PAH, but also of the tyrosine and tryptophan hydroxylases. 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 tetrahydropterine synthase deficiency, dihydropyridine 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 mental retardation 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 that derives 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 60.6 = result in nmol/mL

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 55.6 = 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


**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 using methanol:water (50:50) solution containing the IS. The mixture is vortexed and centrifuged to precipitate protein. The supernatant is diluted and then introduced into the tandem mass spectrometer (MS/MS). Chromatography is performed using a C18 (150x4.6mm) column. The concentration of Phe and Tyr are established by comparison of the ion intensity with that of the IS (d5-Phe and Tyr, respectively).(Unpublished Mayo method)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Monday through Friday; 1 p.m.

**Analytic Time**

3 days (not reported on Saturday or Sunday)

**Maximum Laboratory Time**

5 days

**Specimen Retention Time**

2 weeks

**Performing Laboratory Location**

Rochester

**Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

**CPT Code Information**

84030-Phenylalanine

84510-Tyrosine

**LOINC® Information**
# Test Definition: PKU
Phenylalanine and Tyrosine, P

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