

Overview

Useful For

Differentiating between disorders of peroxisomal biogenesis (eg, Zellweger syndrome) and disorders with loss of a single peroxisomal function

Detecting abnormal elevations of pipecolic acid in serum

Genetics Test Information

In the newborn period, pipecolic acid levels are more likely to be abnormal in urine than in plasma or serum. Abnormal levels of pipecolic acid should be interpreted together with the results of other biochemical markers of peroxisomal disorders, such as plasma C22-C26 very long-chain fatty acids, phytanic acid, pristanic acid, red blood cell plasmalogens, and bile acid intermediates.

Testing Algorithm

See [Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#) in Special Instruction.

Special Instructions

- [Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#)

Highlights

Measurement of pipecolic acid is a useful diagnostic tool for differentiating between peroxisomal biogenesis disorders (Zellweger spectrum disorders) and peroxisomal disorders caused by single enzyme deficiencies such as X-linked adrenoleukodystrophy.

Results must be interpreted together with the results of other biochemical markers for peroxisomal disorders.

Both urine and plasma are suitable specimens for the detection of pipecolic acid.

Method Name

Gas Chromatography-Mass Spectrometry (GC-MS)

NY State Available

Yes

Specimen

Specimen Type

Serum

Necessary Information

Patient's age is required.

Specimen Required

Patient Preparation: Fasting 12 hours or more. (Collect specimens from infants and small children just before next feeding)

Collection Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Submission Container/Tube: Plastic vial

Specimen Volume: 1.5 mL

Collection Instructions: Centrifuge and aliquot serum into plastic vial.

Forms

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

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	94 days	
	Refrigerated	14 days	

Clinical & Interpretive**Clinical Information**

Pipecolic acid (PA) is an intermediate of lysine metabolism and is oxidized in the peroxisomes by the enzyme L-pipecolate oxidase. In peroxisome biogenesis disorders (eg, Zellweger syndrome), the activity of this enzyme is lost, resulting in an increase in pipecolic acid levels. In contrast, in peroxisomal disorders involving single enzyme deficiencies such as D-bifunctional protein deficiency, PA is not elevated; therefore, PA analysis is useful for differentiating between these 2 groups of disorders.

Increased pipecolic acid levels may also be seen in alpha-amino adipic semialdehyde dehydrogenase deficiency (pyridoxine-dependent epilepsy), hyperlysinemia types 1 and 2, and defects in proline metabolism.

Theoretically, a defect in L-pipecolate oxidase can exist and several cases of hyperpipecolic acidemia have been reported, but a specific enzyme deficiency has not been described in any of the patients.

Reference Values

<6 months: < or =6.0 nmol/mL

6 months-<1 year: < or =5.9 nmol/mL

1-17 years: < or =4.3 nmol/mL

> or =18 years: < or =7.4 nmol/mL

Interpretation

Elevated pipecolic acid levels are seen in disorders of peroxisomal biogenesis; normal levels are seen in disorders with loss of a single peroxisomal function.

Abnormal levels of pipecolic acid should be interpreted together with the results of other biochemical markers of peroxisomal disorders, such as plasma C22-C26 very long-chain fatty acids, phytanic acid, and pristanic acid (POX / Fatty Acid Profile, Peroxisomal [C22-C26], Serum); red blood cell plasmalogens; and bile acid intermediates.

Cautions

Newborns with disorders of peroxisomal biogenesis often have normal levels of pipecolic acid that increase with age.

Abnormal results may reflect either prematurity or nongenetic liver and/or renal disease.

Vigabatrin interferes with pipecolic acid determination.

Methylmalonic acid interferes with pipecolic acid determination.

Clinical Reference

1. Gartner J, Rosewich H, Thoms S: The peroxisome biogenesis disorders. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. *The Online Metabolic and Molecular Bases of Inherited Disease*. McGraw-Hill Medical; 2019. Accessed May 18, 2021. Available at www.ommbid.com
2. Wanders RJA, Barth PG, Heymans HAS: Single peroxisomal enzyme deficiencies. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. *The Online Metabolic and Molecular Bases of Inherited Disease*. McGraw-Hill Medical; 2019. Accessed May 18, 2021. Available at www.ommbid.com
3. Peduto A, Baumgartner MR, Verhoeven NM: Hyperpipecolic acidemia: a diagnostic tool for peroxisomal disorders. *Mol Genet Metab*. 2004 Jul;82(3):224-230
4. Braverman N, Raymond G, Rizzo WB, et al: Peroxisome biogenesis disorders in the Zellweger spectrum: An overview of current diagnosis, clinical manifestations, and treatment guidelines. *Mol Genet Metab*. 2016 Mar;117(3):313-321

Performance**Method Description**

Pipecolic acid is quantitated by a stable isotope dilution method; electron capture negative chemical ionization gas chromatography-mass spectrophotometry of pentafluorobenzyl esters.(Kok RM, Kaster L, de Jong AP, et al: Stable isotope dilution analysis of pipecolic acid in cerebrospinal fluid, plasma, urine and amniotic fluid using electron capture negative ion mass fragmentography. *Clin Chim Acta*. 1987;168:143-152, Kuhara t, Akiyama T, Ohse M, et al: Identification of new biomarkers of pyridoxine-dependent epilepsy by GC/MS-based urine metabolomics. *Anal Biochem*. 2020 Sep 1;604:113739. doi: 10.1016/j.ab.2020.113739)

PDF Report

No

Day(s) Performed

Thursday

Report Available

2 to 9 days

Specimen Retention Time

1 month

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 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 US Food and Drug Administration.

CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PIPA	Pipecolic Acid, S	32334-5

Result ID	Test Result Name	Result LOINC® Value
81326	Pipecolic Acid, S	32334-5
29964	Reviewed By	18771-6
29962	Interpretation	59462-2