MAYO CLINIC LABORATORIES

Test Definition: PIPU

Pipecolic Acid, Random, Urine

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 urine

Genetics Test Information

Pipecolic acid is not detected by conventional organic acid analysis of urine.

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

For more information see Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm.

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

Urine

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Necessary Information

Patient's age is required.

Specimen Required

Supplies: Urine tubes, 10 mL (T068)
Container/Tube: Plastic, 10-mL urine tube
Specimen Volume: 5 mL
Collection Instructions:
1. Collect a random urine specimen.
2. No preservative.

Forms

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

Specimen Minimum Volume

2 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	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-aminoadipic 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

< or =31 days: < or =223.8 nmol/mg creatinine
32 days-5 months: < or =123.1 nmol/mg creatinine

6 months-11 months: < or =45.0 nmol/mg creatinine
> or =1 year: < or =5.7 nmol/mg creatinine

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 serum C22-C26 very long-chain fatty acids, phytanic acid, pristanic acid (POX / Fatty Acid Profile, Peroxisomal [C22-C26], Serum); red blood cell plasmalogens (PGRBC / Plasmalogens, Blood); and bile acid intermediates (BAIPD / Bile Acids for Peroxisomal Disorders, Serum).

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 or kidney disease.

Pipecolic acid is not detected by conventional organic acid analysis (OAU / Organic Acids Screen, Random, Urine).

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 July 30, 2025. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=22554226
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 July 30, 2025. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225542524
3. Peduto A, Baumgartner MR, Verhoeven NM, et al. Hyperpipecolic acidaemia: a diagnostic tool for peroxisomal disorders. Mol Genet Metab. 2004;82:224-230
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;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;604:113739. doi:10.1016/j.ab.2020.113739)

PDF Report
No

Day(s) Performed
Tuesday

Report Available
3 to 9 days

Specimen Retention Time
1 month

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
82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PIPU	Pipecolic Acid, U	33659-4

Result ID	Test Result Name	Result LOINC® Value
81248	Pipecolic Acid, U	33659-4
29952	Interpretation	59462-2
29954	Reviewed By	18771-6