MAYO CLINIC LABORATORIES

Test Definition: POX

Fatty Acid Profile, Peroxisomal, S

Overview

Useful For

Evaluating patients with possible peroxisomal disorders, single-enzyme defects of peroxisomal metabolism such as X-linked adrenoleukodystrophy or peroxisomal biogenesis disorders (Zellweger syndrome spectrum) using serum specimens

Aiding in the assessment of peroxisomal function

Testing Algorithm

The following algorithms are available in Special Instructions:

-Newborn Screen Follow-up for X-Linked Adrenoleukodystrophy

-Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm

For more information, see Newborn Screening Act Sheet X-Linked Adrenoleukodystrophy: Increased Very Long Chain Fatty Acids in Special Instructions.

Special Instructions

- Newborn Screening Act Sheet X-linked Adrenoleukodystrophy: Increased Very Long Chain Fatty Acids
- Newborn Screen Follow-up for X-Linked Adrenoleukodystrophy
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Highlights

This test analyzes very long-chain fatty acids as well as pristanic and phytanic acid to aid in diagnosis of peroxisomal biogenesis disorders, X-linked adrenoleukodystrophy (X-ALD), and Refsum disease.

This test is also appropriate for follow-up of an abnormal newborn screen for X-ALD.

Reports include concentrations of C22:0, C24:0, C26:0 species, phytanic acid and pristanic acid, and calculated C24:0/C22:0, C26:0/C22:0, and phytanic acid/pristanic acid ratios.

Method Name

Gas Chromatography-Mass Spectrometry (GC-MS) Stable Isotope Dilution Analysis

NY State Available

Yes

Specimen

Specimen Type

Serum

Necessary Information

1. Patient's age and sex is required.

2. Include information regarding treatment, family history, and tentative diagnosis.

Specimen Required

Patient Preparation:

1. Fasting-overnight (12-14 hours). If fasting not possible for babies or infants, collect specimen prior to next feeding.

2. Patient must not consume any alcohol for 24 hours before the specimen is collected.

Collection Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 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.

Reject Due To

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

Specimen Minimum Volume

0.15 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	92 days	
	Refrigerated	15 days	

Clinical & Interpretive

Clinical Information

Peroxisomes are organelles present in all human cells except mature erythrocytes. They carry out essential metabolic functions including beta-oxidation of very long-chain fatty acids (VLCFA), alpha-oxidation of phytanic acid, and biosynthesis of plasmalogen and bile acids. Peroxisomal disorders include disorders of peroxisomal biogenesis with defective assembly of the entire organelle and single peroxisomal enzyme/transporter defects where the organelle is intact, but a specific function is disrupted. Peroxisomal beta-oxidation of VLCFA is impaired in all disorders of peroxisomal biogenesis and in selected single enzyme deficiencies, particularly X-linked adrenoleukodystrophy (X-ALD), resulting in elevated concentrations of VLCFA in plasma or serum.

Peroxisomal biogenesis disorders (PBD) include the Zellweger syndrome spectrum disorders, which are clinically diverse and range in severity from neonatal lethal (Zellweger syndrome) to more variable clinical courses in neonatal adrenoleukodystrophy and infantile Refsum disease. Affected children typically have hypotonia, poor feeding, distinctive facial features, seizures, and liver dysfunction. Other features can include retinal dystrophy, hearing loss, developmental delays, and bleeding episodes. Rhizomelic chondrodysplasia punctata is another PBD. It is characterized by rhizomelic shortening, chondrodysplasia punctata, cataracts, intellectual disability, and seizures, although it can have a milder phenotype with only cataracts and chondrodysplasia. The typical biochemical profile shows normal VLCFA and elevated phytanic acid.

X-ALD is a neurologic disorder affecting the white matter and adrenal cortex. It can present between ages 4 and 8 years as a childhood cerebral form with behavioral and cognitive changes, associated with neurologic decline. Other forms include an "Addison disease only" phenotype with adrenocortical insufficiency without initial neurologic abnormality and adrenomyeloneuropathy associated with later-onset progressive paraparesis. X-ALD is an X-linked condition that primarily affects male patients; however, some female patients who are carriers can develop later-onset neurologic manifestations. In 2016, X-ALD was added to the US Recommended Uniform Screening Panel, a list of conditions that are nationally recommended for newborn screening by the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children.

Refsum disease is a peroxisomal disorder characterized by anosmia, retinitis pigmentosa, neuropathy, deafness, ataxia, ichthyosis, and cardiac abnormalities. The classic biochemical profile of Refsum disease is an elevated plasma or serum

phytanic acid level.

Biochemical abnormalities in peroxisomal disorders include accumulations of VLCFA, phytanic, and pristanic acid. The differential diagnosis of these disorders is based on recognition of clinical phenotypes combined with a series of biochemical tests to assess peroxisomal function and structure. These include measurements and ratios of VLCFA, pipecolic acid (PIPA / Pipecolic Acid, Serum; PIPU / Pipecolic Acid, Random, Urine), phytanic acid and its metabolite pristanic acid. In addition, confirmatory testing for X-ALD (XALDZ / X-Linked Adrenoleukodystrophy, Full Gene Analysis, Varies) via molecular genetic analysis is available.

Reference Values

C22:0

< or =96.3 nmol/mL

C24:0

< or =91.4 nmol/mL

C26:0

< or =1.30 nmol/mL

C24:0/C22:0 RATIO

< or =1.39

C26:0/C22:0 RATIO

< or =0.023

PRISTANIC ACID

0-4 months: < or =0.60 nmol/mL

5-8 months: < or =0.84 nmol/mL

9-12 months: < or =0.77 nmol/mL

13-23 months: < or =1.47 nmol/mL

> or =24 months: < or =2.98 nmol/mL

PHYTANIC ACID

0-4 months: < or =5.28 nmol/mL

5-8 months: < or =5.70 nmol/mL

9-12 months: < or =4.40 nmol/mL

13-23 months: < or =8.62 nmol/mL

> or =24 months: < or =9.88 nmol/mL

PRISTANIC/PHYTANIC ACID RATIO

0-4 months: < or =0.35

5-8 months: < or =0.28

9-12 months: < or =0.23

13-23 months: < or =0.24

> or =24 months: < or =0.39

Interpretation

Reports include concentrations of C22:0, C24:0, C26:0 species, phytanic acid and pristanic acid, and calculated C24:0/C22:0, C26:0/C22:0, and phytanic acid:pristanic acid ratios. When no significant abnormalities are detected, a simple descriptive interpretation is provided.

A profile of elevated phytanic acid, low-normal pristanic acid, and normal very long-chain fatty acids is suggestive of Refsum disease (phytanic acid oxidase deficiency); however, serum phytanic acid concentration may also be increased in disorders of peroxisomal biogenesis and should be considered in the differential diagnosis of peroxisomal disorders.

If results are suggestive of hemizygosity for X-linked adrenoleukodystrophy, we also include the calculated value of a discriminating function used to more accurately segregate hemizygous individuals from normal controls.

Positive test results could be due to a genetic or nongenetic condition. Additional confirmatory testing would be required to differentiate between these causes.

Cautions

In rare instances, patients with X-linked adrenoleukodystrophy (X-ALD) may have only minimally elevated values; 15% to 20% of women heterozygous for X-ALD have normal plasma very long-chain fatty acid levels.

False-positive results may occur with nonfasting specimens.

Clinical Reference

1. Moser AB, Kreiter N, Bezman L, et al: Plasma very long chain fatty acid assay in 3,000 peroxisome disease patients and 29,000 controls. Ann Neurol. 1999;45:100-110

2. Turk BR, Theda C, Fatemi A, Moser AB: X-linked adrenoleukodystrophy: Pathology, pathophysiology, diagnostic testing, newborn screening and therapies. Int J Dev Neurosci. 2020;80(1):52-72. doi: 10.1002/jdn.10003

3. Waterham HR, Ferdinandusse S, Wanders RJA: Human disorders of peroxisome metabolism and biogenesis. Biochimica et Biophysica Acta. 2016 May;1863(5):922-933. doi: 10.1016/j.bbamcr.2015.11.015

Performance

Method Description

Acidic hydrolysis is followed by basic hydrolysis and reacidification. Hexane extraction then proceeds to derivatization with pentafluorobenzyl bromide (PFB). Separation and detection of PFB-esters is accomplished by capillary gas chromatography-mass spectrometry using electron capture ionization and selected negative ion monitoring. Quantitation is enhanced by the use of stable isotope-labeled internal standards.(Stellard F, ten Brink HJ, Kok RM, et al: Stable isotope dilution analysis of very long chain fatty acids in plasma, urine and amniotic fluid by electron capture negative ion mass fragmentography. Clin Chim Acta. 1990;192:133-144, Rattay TW, Rautenberg M, Sohn AS, et al: Defining diagnostic cutoffs in neurological patients for serum very long chain fatty acids (VLCFA) in genetically confirmed X-adrenoleukodystrophy. Sci Rep. 2020 Sep 15;10[1]:15093)

PDF Report

No

Specimen Retention Time
1 month

Performing Laboratory Location
Rochester

Fees & Codes

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
82726

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
POX	Fatty Acid Profile, Peroxisomal, S	43677-4

Result ID	Reporting Name	LOINC®
81369	C22:0	30194-5
7143	C24:0	30195-2
7137	C26:0	30197-8
7138	C24:0/C22:0	30196-0
7139	C26:0/C22:0	30198-6
7140	Pristanic Acid	22761-1
7141	Phytanic Acid	22671-2
7142	Pristanic/Phytanic	30550-8
7144	Comment	48767-8