MAYO CLINIC LABORATORIES

Test Definition: PPFE

Protoporphyrins, Fractionation, Whole Blood

Overview

Useful For

Evaluating patients with possible diagnoses of erythropoietic protoporphyria or X-linked dominant protoporphyria

Establishing a biochemical diagnosis of erythropoietic protoporphyria and X-linked dominant protoporphyria

Testing Algorithm

This test should **not be ordered** in conjunction with PEE / Porphyrins Evaluation, Whole Blood.

The following information is available:
-Porphyria (Acute) Testing Algorithm
-Porphyria (Cutaneous) Testing Algorithm
-The Heme Biosynthetic Pathway

Special Instructions

- The Heme Biosynthetic Pathway
- Porphyria (Acute) Testing Algorithm
- Porphyria (Cutaneous) Testing Algorithm

Method Name

High-Performance Liquid Chromatography (HPLC) with Fluorescence Detection

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This test is for assessment for protoporphyria. The preferred test for lead toxicity in children is blood lead. For more information see PBDV / Lead, Venous with Demographics, Blood or PBDC / Lead, Capillary, with Demographics, Blood. The preferred screening test for suspicion of a hepatic porphyria is urine porphyrins. For more information see PQNRU / Porphyrins, Quantitative, Random, Urine. This test should **not be ordered** with PEE / Porphyrins Evaluation, Whole Blood

Necessary Information

Include a list of medications the patient is currently taking.

Specimen Required

All porphyrin tests on whole blood can be performed on 1 tube.

Patient Preparation: Patient **must not** consume any alcohol for 24 hours before specimen collection.
Container/Tube:
Preferred: Green top (sodium heparin)
Acceptable: Dark blue top (metal free heparin), green top (lithium heparin), or lavender top (EDTA)
Specimen Volume: 4 mL
Collection Instructions: Refrigerate specimen as soon as possible.

Forms

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

Specimen Minimum Volume

3 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information

The porphyrias are a group of inherited disorders resulting from enzyme defects in the heme biosynthetic pathway. Depending on the specific enzyme involved, various porphyrins and their precursors accumulate in different specimen types. The patterns of porphyrin accumulation in erythrocytes and plasma and excretion of the heme precursors in urine and feces allow for the detection and differentiation of the porphyrias.

Testing protoporphyrin fractions is most informative for patients with a clinical suspicion of erythropoietic protoporphyria (EPP) or X-linked dominant protoporphyria (XLDPP). Clinical presentation of EPP and XLDPP is identical with onset of symptoms typically occurring in childhood. Cutaneous photosensitivity in sun-exposed areas of the skin generally worsens in the spring and summer months. Common symptoms may include itching, edema, erythema, stinging or burning sensations, and occasionally scarring of the skin in sun-exposed areas. Although genetic in nature, environmental factors exacerbate symptoms, significantly impacting the severity and course of disease.

Erythropoietic protoporphyria is caused by diminished ferrochelatase resulting in significantly increased free protoporphyrin levels in erythrocytes, plasma, and feces.

X-linked dominant protoporphyria is caused by gain-of-function variants in the C-terminal end of *ALAS2* gene and results

in elevated erythrocyte levels of free and zinc-complexed protoporphyrin in erythrocytes, and total protoporphyrin levels in plasma and feces.

Other possible causes of elevated erythrocyte zinc-complexed protoporphyrin may include:
-Iron-deficiency anemia, the most common cause
-Chronic intoxication by heavy metals (primarily lead) or various organic chemicals
-Congenital erythropoietic porphyria, a rare autosomal recessive porphyria caused by deficient uroporphyrinogen III synthase
-Hepatoerythropoietic porphyria, a rare autosomal recessive porphyria caused by deficient uroporphyrinogen decarboxylase

Typically, the workup of patients with a suspected porphyria is most effective when following a stepwise approach. See Porphyria (Acute) Testing Algorithm and Porphyria (Cutaneous) Testing Algorithm or call 800-533-1710 to discuss testing strategies.

There are 2 test options:
-PPFE / Protoporphyrins, Fractionation, Whole Blood
-PPFWE / Protoporphyrins, Fractionation, Washed Erythrocytes
The whole blood option is easiest for clients but requires that the specimen arrive at Mayo Clinic Laboratories within 7 days of collection. When this cannot be ensured, washed frozen erythrocytes, which are stable for 14 days, should be submitted.

Reference Values

FREE PROTOPORPHYRIN
<20 mcg/dL

ZINC-COMPLEXED PROTOPORPHYRIN
<60 mcg/dL

Interpretation

Abnormal results are reported with a detailed interpretation that may include an overview of the results and their significance, a correlation to available clinical information provided with the specimen, differential diagnosis, and recommendations for additional testing when indicated and available.

Cautions

Patients must abstain from alcohol for at least 24 hours prior to specimen collection. Alcohol suppresses enzyme activity potentially leading to false-positive results.

Clinical Reference

1. Tortorelli S, Kloke K, Raymond K. Disorders of porphyrin metabolism. In: Dietzen DJ, Bennett MJ, Wong EDD, eds. Biochemical and Molecular Basis of Pediatric Disease. 4th ed. AACC Press; 2010:307-324
2. Phillips JD. Heme biosynthesis and the porphyrias. Mol Genet Metab. 2019;128(3):164-177. doi:10.1016/j.ymgme.2019.04.008
3. Anderson KE, Sassa S, Bishop DF, Desnick RJ. Disorders of heme biosynthesis: X-Linked sideroblastic anemia and the porphyrias. 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 September 6, 2024. Available at

https://ommbid.mhmedical.com/content.aspx?sectionid=225540906&bookid=2709
4. Whatley SD, Ducamp S, Gouya L, et al. C-terminal in the *ALAS2* gene lead to gain of function and cause X-linked dominant protoporphyria without anemia or iron overload. Am J Hum Genet. 2008;83(3):408-414

Performance

Method Description
Extraction followed by fractionation by high-performance liquid chromatography. Zinc protoporphyrin and free protoporphyrin are separately quantitated.(Smith RM, Doran D, Mazur M, Bush B. High-performance liquid chromatographic determination of protoporphyrin and zinc protoporphyrin in blood. J Chromatogr.1980;181[3-4]:319-327; Gou EE, Balwani M, Bissell DM, et al. Pitfalls in erythrocyte protoporphyrin measurement for diagnosis and monitoring of protoporphyrias. Clin Chem. 2015;61[12]:1453-1456. doi:10.1373/clinchem.2015.245456)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
3 to 5 days

Specimen Retention Time
14 days

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 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
PPFE	Protoporphyrins, Fractionation, WB	94490-0

Result ID	Test Result Name	Result LOINC® Value
2327	Zinc-Complexed Protoporphyrin	2895-1
2326	Free Protoporphyrin	94491-8
29511	Interpretation	59462-2