

## Overview

### Useful For

Preferred test for analysis of erythrocyte protoporphyrin fractions

Preferred test for evaluating patients with possible diagnoses of erythropoietic protoporphyria and X-linked dominant protoporphyria

Establishing a biochemical diagnosis of erythropoietic protoporphyria, or X-linked dominant protoporphyria

### Testing Algorithm

This test should **not** be ordered in conjunction with PEWE / Porphyrins Evaluation, Washed Erythrocytes.

The following algorithms are available in Special Instructions:

[-Porphyria \(Acute\) Testing Algorithm](#)

[-Porphyria \(Cutaneous\) Testing Algorithm](#)

### 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

Washed RBC

### Ordering Guidance

This test is for assessment for protoporphyria, an erythropoietic porphyria. 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.

### Necessary Information

1. **Volume of packed cells and total volume of erythrocyte suspension (red cells + saline) are required and must be sent with specimen.**
2. Include a list of medications the patient is currently taking.

### Specimen Required

All porphyrin tests on erythrocytes can be performed on 1 tube.

**Patient Preparation:** Patient should abstain from alcohol for 24 hours.

**Collection Container/Tube:**

**Preferred:** Green top (sodium heparin)

**Acceptable:** Dark blue top (metal free heparin) or green top (lithium heparin)

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** Washed erythrocyte suspension

**Collection Instructions:** Collect and process whole blood specimen as follows:

1. Transfer entire specimen to a 12-mL graduated centrifuge tube.
2. Centrifuge specimen for 10 minutes at 2000 rpm.
3. **Record volume of packed cells and the total volume of the specimen.**
4. Discard supernatant plasma.
5. Wash packed erythrocytes 2 times by resuspension of at least an equal amount of cold 0.9% saline, mix, and centrifuge for 5 minutes at 2000 rpm, discarding supernatant after each washing.
6. Resuspend packed cells to the original total volume with 0.9% saline. Invert specimen gently to mix.
7. Transfer washed erythrocytes into a plastic vial and freeze.

### Forms

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

### Reject Due To

Other Cell suspension not available

### Specimen Minimum Volume

1 mL

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Washed RBC	Frozen (preferred)	14 days	
	Refrigerated	14 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.

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

XLDPP is caused by gain-of-function variants in the C-terminal end of *ALAS2* gene and results in elevated erythrocyte

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levels of free and zinc-complexed protoporphyrin, and total protoporphyrin 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 (CEP), a rare autosomal recessive porphyria caused by deficient uroporphyrinogen III synthase
- Hepatoerythropoietic porphyria (HEP), 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](#) in Special Instructions 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. Alcohol suppresses enzyme activity potentially leading to false-positive results.

### Clinical Reference

1. Tortorelli S, Kloke K, Raymond K: Chapter 15: Disorders of porphyrin metabolism. *In* Biochemical and Molecular Basis of Pediatric Disease. Fourth edition. Edited by DJ Dietzen, MJ Bennett, ECC Wong. AACCC Press 2010, pp 307-324
2. Nuttall KL, Klee GG: Analytes of hemoglobin metabolism-porphyrins, iron, and bilirubin. *In* Tietz Fundamentals of Clinical Chemistry. Fifth edition. Edited by CA Burtis, ER Ashwood. Philadelphia, WB Saunders Company, 2001, pp 584-607
3. Anderson KE, Sassa S, Bishop DF, Desnick RJ: Disorders of Heme Biosynthesis: X-Linked Sideroblastic Anemia and the Porphyrins. *In* The Online Metabolic and Molecular Bases of Inherited Disease. Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York, McGraw-Hill. Accessed August 2, 2019. Available at <http://ommbid.mhmedical.com/content.aspx?bookid=971&Sectionid=62638866>
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 Sep;83(3):408-414

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**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 Mar 14;181[3-4]:319-327; Gou EE, Balwani M, Bissell DM, et al: Pitfalls in Erythrocyte Protoporphyrin Measurement for Diagnosis and Monitoring of Protoporphyrin. Clin Chem. 2015 Dec;61[12]:1453-6. doi: 10.1373/clinchem.2015.245456)

**PDF Report**

No

**Specimen Retention Time**

2 weeks

**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**

82542