MAYO CLINIC LABORATORIES

Test Definition: PEE

Porphyrins Evaluation, Whole Blood

Overview

Useful For

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

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
PPFE	Protoporphyrins, Fractionation, WB	Yes	No

Testing Algorithm

This test is recommended for screening patients for possible erythropoietic protoporphyria and X-linked dominant protoporphyria. In addition, it can be used for evaluation of iron-deficiency anemia and chronic lead intoxication. Testing begins with total erythrocyte porphyrins. If the result is below 80 mcg/dL, it is normal, and testing is complete.

If the total erythrocyte porphyrin value is 80 mcg/dL or above, the protoporphyrin fractionation assay will automatically be performed at an additional charge. The fractionation test results include noncomplexed (free) protoporphyrin and zinc-complexed protoporphyrin.

The following algorithms are available:
-Porphyria (Acute) Testing Algorithm
-Porphyria (Cutaneous) Testing Algorithm

Special Instructions

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

Method Name

Spectrofluorometric

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This is the preferred test for assessment for protoporphyria. The preferred test for assessing 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

Include a list of medications the patient is currently taking.

Specimen Required

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

Patient Preparation: Patient **must not** consume any alcohol for 24 hours before specimen collection.
Container/Tube:
Preferred: Green top (sodium heparin)
Acceptable: Lavender top (EDTA), dark blue top (metal free heparin), royal blue top (metal free EDTA), green top (lithium heparin)
Specimen Volume: 4 mL
Collection Instructions: Immediately place specimen on wet ice.

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 erythrocyte porphyrin level 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 can exacerbate symptoms, significantly impacting the severity and course of disease.

Erythropoietic protoporphyria is caused by decreased ferrochelatase activity resulting in significantly increased noncomplexed (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, and total protoporphyrin levels in plasma and feces.

Protoporphyrin fractionation is the main component of erythrocyte porphyrins. When total erythrocyte porphyrins are elevated, fractionation and quantitation of zinc-complexed and free protoporphyrin is necessary to differentiate the inherited porphyrias from other causes of elevated porphyrin levels. 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:
-PEE / Porphyrins Evaluation, Whole Blood
-PEWE / Porphyrins Evaluation, 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

PORPHYRINS, TOTAL, RBC
<80 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

Alcohol suppresses enzyme activity potentially leading to false-positive results if it is ingested within 24 hours of

specimen collection.

Clinical Reference

1. Tortorelli S, Kloke K, Raymond K. Disorders of porphyrin metabolism. In: Dietzen DG, Bennett MJ, Wong ECC, eds. Biochemical and Molecular Basis of Pediatric Disease. 4th ed. AACC Press; 2010:307-324
2. Badminton MN, Whatley SD, Schmitt C, Aarsand AK. Porphyrins and the porphyrias. In: Rifai N, Chiu RWK, Young I, Burnham CAD, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:419-419.e32
3. Anderson KE, Sassa S, Bishop DF, Desnick RJ. Disorders of heme biosynthesis: X-linked sideroblastic anemia and the porphyrias In: Valle D, 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 B, et al. C-terminal deletions 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
5. Balwani M, Naik H, Anderson KE, et al. Clinical, biochemical, and genetic characterization of North American patients with erythropoietic protoporphyria and X-linked protoporphyria. JAMA Dermatol. 2017;153(8):789-796

Performance

Method Description

This evaluation is performed as a 2-step analysis. First, the total red blood cell (RBC) porphyrin concentration is determined by extracting the porphyrins from washed, resuspended RBCs using a mixture of ethyl acetate and acetic acid. The porphyrins are then back extracted into dilute hydrochloric acid. Total porphyrins are quantified using this extract via spectrofluorometry.(Piomelli S. Free erythrocyte porphyrins in the detection of undue absorption of Pb and Fe deficiency. Clin Chem. 1977;23:264-269; 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)

If the total porphyrin concentration is elevated, the RBCs are re-extracted to separate and quantify the zinc-complexed and noncomplexed (free) protoporphyrin via high-performance liquid chromatography.(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

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

84311
82542-if appropriate

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PEE	Porphyrins Evaluation, WB	2814-2

Result ID	Test Result Name	Result LOINC® Value
88886	Total Porphyrins, WB	2814-2
29356	Interpretation	59462-2