MAYO CLINIC LABORATORIES

# Test Definition: PQNU

Porphyrins, Quantitative, 24 Hour, Urine

## Overview

### Useful For

Preferred screening test for congenital erythropoietic porphyria and porphyria cutanea tarda and during symptomatic periods for acute intermittent porphyria, hereditary coproporphyria, and variegate porphyria when specimen transport **will be longer than 72 hours**

### Genetics Test Information

This test is preferred during symptomatic periods for acute intermittent porphyria, hereditary coproporphyria, and variegate porphyria when specimen transport will be longer than 72 hours. If the specimen will be received at Mayo Clinic Laboratories within 72 hours of collection, PQNRU / Porphyrins, Quantitative, Random, Urine is recommended.

Testing includes porphobilinogen, which is useful in the evaluation of the acute porphyrias.

This is the preferred test to begin assessment for congenital erythropoietic porphyria and porphyria cutanea tarda.

### Testing Algorithm

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

### Special Instructions

- The Heme Biosynthetic Pathway
- Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens
- Porphyria (Acute) Testing Algorithm
- Porphyria (Cutaneous) Testing Algorithm

### Method Name

High-Performance Liquid Chromatography (HPLC) with Fluorometric Detection/Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Urine

### Ordering Guidance

This 24-hour urine test should be ordered when the specimen **will not** reach Mayo Clinic Laboratories (MCL) within 72

hours. If the specimen **will** reach MCL within 72 hours, order PQNRU / Porphyrins, Quantitative, Random, Urine.

## Shipping Instructions

Ship specimen in amber container to protect from light.

## Necessary Information

**1. 24-Hour volume (in milliliters) is required.**

**2. Patient's sex is required.**

3. Collection date and time should be documented upon completion of the 24-hour collection.

4. Include a list of medications the patient is currently taking.

## Specimen Required

**Patient Preparation:** Patient **should not** consume any alcohol for the 24 hours before, as well as during, specimen collection.

**Supplies:**

-Urine Container - Amber, 60-mL (T596)

-Sodium Carbonate, 5 gram (T272)

**Container/Tube:** Amber**,** 60-mL urine container

**Specimen Volume:** 20 to 50 mL

**Collection Instructions:**

1. Collect a 24-hour urine specimen.

2. Add 5 g of sodium carbonate as preservative at start of collection. This preservative is intended to achieve a pH above

7. **Do not substitute sodium bicarbonate for sodium carbonate.**

3. The container should be refrigerated and protected from light as much as possible during collection. An aliquot should be frozen when collection is complete.

**Additional Information:** See Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens for multiple collections.

## Forms

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

## Urine Preservative Collection Options

**Note:** The addition of preservative must occur prior to beginning the collection.

| | |
|---|---|
| Ambient | No |
| Refrigerate | No |
| Frozen | No |
| 50% Acetic Acid | No |
| Boric Acid | No |
| Diazolidinyl Urea | No |
| 6M Hydrochloric Acid | No |
| 6M Nitric Acid | No |
| Sodium Carbonate | Required |
| Thymol | No |
| Toluene | No |
| **Protect specimen from light. | |

### Specimen Minimum Volume

15 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 | 7 days | LIGHT PROTECTED |

## 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.

The porphyrias are typically classified as erythropoietic or hepatic based upon the primary site of the enzyme defect. In addition, hepatic porphyrias can be further classified as chronic or acute, based on their clinical presentation.

The primary acute hepatic porphyrias: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), and variegate porphyria (VP), are associated with neurovisceral symptoms that typically onset during puberty or later. Common symptoms include severe abdominal pain, peripheral neuropathy, and psychiatric symptoms. Crises may be precipitated by a broad range of medications (including barbiturates and sulfa drugs), alcohol, infection, starvation, heavy metals, and hormonal changes. Photosensitivity is not associated with AIP but may be present in HCP and VP.

Cutaneous photosensitivity is associated with the chronic hepatic porphyrias: porphyria cutanea tarda (PCT) and the erythropoietic porphyrias; erythropoietic protoporphyria (EPP), X-linked dominant protoporphyria (XLDPP), and congenital erythropoietic porphyria (CEP). Although genetic in nature, environmental factors may exacerbate symptoms, significantly impacting the severity and course of disease.

CEP is an erythropoietic porphyria caused by uroporphyrinogen III synthase deficiency. Symptoms typically present in early infancy with red-brown staining of diapers, severe cutaneous photosensitivity with fluid-filled bullae and vesicles. Other common symptoms may include thickening of the skin, hypo- and hyperpigmentation, hypertrichosis, cutaneous scarring, and deformities of the fingers, eyelids, lips, nose, and ears. A few milder adult-onset cases have been documented as well as cases that are secondary to myeloid malignancies.

PCT is the most common form of porphyria and caused by hepatic inhibition of the enzyme uroporphyrinogen decarboxylase (UROD). It is most often sporadic (acquired), but in about 20% of cases, a heterozygous variant in *UROD* increases the susceptibility to disease. The most prominent clinical characteristics are cutaneous photosensitivity and scarring on sun-exposed surfaces. Patients experience chronic blistering lesions resulting from mild trauma to

sun-exposed areas. These fluid-filled vesicles rupture easily, become crusted, and heal slowly. Secondary infections can cause areas of hypo- or hyperpigmentation or sclerodermatous changes and may result in the development of alopecia at sites of repeated skin damage. Liver disease is common in patients with PCT as evidenced by abnormal liver function tests and with 30% to 40% of patients developing cirrhosis. In addition, there is an increased risk of hepatocellular carcinoma.

Hepatoerythropoietic porphyria (HEP) is a rare autosomal recessive form of porphyria caused by homozygous or compound heterozygous variants in *UROD.* It typically presents in early childhood with both erythropoietic and cutaneous manifestations and is similar to what is seen in CEP.

Urinary porphyrin determination is helpful in the diagnosis of most porphyrias including CEP, PCT, AIP, HCP, and VP. In addition, measurement of porphobilinogen (PBG) in urine is important in establishing the diagnosis of the acute neurologic porphyrias (AIP, HCP and VP). Neither urine porphyrins nor PBG is helpful in evaluating patients suspected of having EPP or XLDPP.

Of note, porphyrinuria may result from exposure to certain drugs and toxins or other medical conditions (ie, hereditary tyrosinemia type I). Heavy metals, halogenated solvents, various drugs, insecticides, and herbicides can interfere with heme production and cause "intoxication porphyria." Chemically, the intoxication porphyrias are characterized by increased excretion of uroporphyrin and/or coproporphyrin in urine.

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.

## Reference Values

UROPORPHYRINS (OCTACARBOXYL):
< or =30 nmol/24 hours

HEPTACARBOXYLPORPHYRINS:
< or =9 nmol/24 hours

HEXACARBOXYLPORPHYRINS:
< or =8 nmol/24 hours

PENTACARBOXYLPORPHYRINS:
< or =10 nmol/24 hours

COPROPORPHYRINS (TETRACARBOXYL)
Males: < or =230 nmol/24 hours
Females: < or =168 nmol/24 hours

PORPHOBILINOGEN:
< or =2.2 mcmol/24 hours

## Interpretation

Abnormal results are reported with a detailed interpretation which 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

Urine preservative should be used; 24-hour collections should be preserved by adding 5.0 g of sodium carbonate to a light-resistant collection container prior to beginning collection. Porphobilinogen (PBG) and porphyrins are susceptible to degradation at high temperature, at pH below 5.0, and on exposure to light.

Neither erythropoietic protoporphyria nor X-linked dominant protoporphyria are detected utilizing urine porphyrins and PBG measurements.

Ethanol and a variety of medications are known to interfere with heme synthesis leading to elevations in urine porphyrins, particularly coproporphyrin. Coproporphyrin elevation without concomitant PBG elevation should not be used as the basis for the diagnosis of porphyria but may warrant follow-up testing with fecal porphyrin analysis.

### 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. Nuttall KL, Klee GG. Analytes of hemoglobin metabolism-porphyrins, iron, and bilirubin. In: Burtis CA, Ashwood ER, eds. Tietz Textbook of Clinical Chemistry. 5th ed. WB Saunders Company; 2001:584-607
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 May 6, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225540906&bookid=2709
4. Weiss Y, Chen B, Yasuda M, Nazarenko I, Anderson KE, Desnick RJ. Porphyria cutanea tarda and hepatoerythropoietic porphyria: Identification of 19 novel uroporphyrinogen III decarboxylase mutations. Mol Genet Metab. 2019;128(3):363-366. doi:10.1016/j.ymgme.2018.11.013

## Performance

### Method Description

An aliquot of urine is acidified and mesoporphyrin is added as an injection marker. Porphyrins in the acidified urine are separated by high-performance liquid chromatography, and the eluted porphyrins are quantified by comparison of their fluorescence intensity to that of known porphyrin standards.(Ford RE, Ou CN, Ellefson RD. Liquid chromatographic analysis for urinary porphyrins. Clin Chem. 1981;27[3]:397-401; de Andrade VL, Mateus ML, Aschner M, Dos Santos AM. Assessment of occupational exposures to multiple metals with urinary porphyrin profiles. J Integr OMICS. 2018;8(1):216. doi:10.5584/jiomics.v8i1.216)

Porphobilinogen (PBG) in urine is quantified by liquid chromatography tandem mass spectrometry after addition of stable isotope-labeled PBG internal standard and solid-phase extraction.(Ford RE, Magera MJ, Kloke KM, et al. Quantitative measurement of porphobilinogen in urine by stable-isotope dilution liquid chromatography-tandem mass spectrometry. Clin Chem. 2001;47[9]:1627-1632; Louleb M, Galvan I, Latrous L, et al. Detection of porphyrins in hair using capillary liquid chromatography-mass spectrometry. Int J Mol Sci. 2022;23(11):6230. doi:10.3390/ijms23116230)

### PDF Report
No

### Day(s) Performed
Monday through Friday

### Report Available
2 to 4 days

### Specimen Retention Time
1 week

### 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
84110-Porphobilinogen, quantitative
84120-Porphyrins, quantitation and fractionation

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| PQNU | Porphyrins, QN, U | 43116-3 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| TM3 | Collection Duration | 13362-9 |
| VL1 | Urine Volume | 3167-4 |
| 29357 | Uroporphyrin, Octa | 15096-1 |
| 29358 | Heptacarboxylporphyrins | 25434-2 |
| 29359 | Hexacarboxylporphyrins | 25438-3 |
| 29360 | Pentacarboxylporphyrins | 25494-6 |
| 29361 | Coproporphyrin, Tetra | 15041-7 |
| 29362 | Porphobilinogen | 14882-5 |

| | | |
|---|---|---|
| 23403 | Interpretation | 59462-2 |