

Porphyrias

Classification of Porphyria:

Primary Porphyria	
Erythropoietic forms	Inherited erythropoietic porphyria, Morbus Günther: Uroporphyrinogen-III co-synthase deficiency, extremely rare, red coloring of teeth, in early childhood light dermatosis, hemolytic anemia, hepatosplenomegaly and deep red urine;
Hepatic forms	Acute intermittent porphyria (AIP): uroporphyrinogen synthase deficiency, the most frequent (approx. 60% of all porphyrias) and most serious porphyria, more women than men affected (4:1), predominant manifestation age: 20-40 th year of life, colic-like abdominal pains, vomiting, crises after drug intake;
Inherited coproporphyria	coproporphyrin oxidase deficiency, very rare, porphyrin in stool increased in latency phases as well;
Porphyria variegata (PV)	protoporphyrinogen oxidase deficiency, rare, manifestation between 10 and 30 years, frequently latent, fecal porphyrin excretion increased;
Porphyria cutanea tarda (PCT)	uroporphyrinogen decarboxylase deficiency, second most frequent porphyria, approx. 35% of all porphyrias, more men than women concerned (3:1), onset usually after 40 years, often after alcohol abuse. Liver function tests are pathological, fecal porphyrins only slightly increased, heptacarboxyporphyrin detectable in stool;
Erythrohepatic forms	Erythrohepatic protoporphyria (EPP): ferrochelatase deficiency, onset at any age, high protoporphyrin excretion in stool, coproporphyrins and uroporphyrins in erythrocytes increased or normal;

Medication induced porphyria	aluminum salts, antiepileptics (carbamazepine, phenytoin, primidone), meprobamate, antirheumatics (gold derivatives, phenacetin, phenylbutazone), danazol, diclofenac, furosemide, griseofulvin, hypnotics and sedatives (esp. barbiturates), local anesthetics, alpha-methyldopa, metopirone, muscle relaxants, anesthetics, spironolactone, sulfonyl urea substances, sulfonamide antibiotics, theophylline, valproic acid, cytostatics;
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Secondary Porphyria	
Intoxications	alcohol, chemicals, heavy metals, (esp. lead: ALS and coproporphyrins in urine, protoporphyrin in urine, stool and in erythrocytes increased);
Liver disorders	cirrhosis, hepatitis, fatty liver, cholestasis, liver changes due to alcohol, porphyrinuria syndrome, hemochromatosis, medication induced damages;
Blood disorders	hemolytic, medication induced, sideroachrestic, sideroplastic and aplastic anemias, malignant anemia, leukemia;
Medication side effects	analgesics, antibiotics, hypnotics, anesthetics, estrogens, sedatives, sulfonyl ureas;
Other causes	diabetes mellitus, neoplasia, iron metabolism disturbances, hepatic cellular bilirubin transport disturbances;

Follow up tests: blood differential, hematocrit, iron, lead, glucose, (postprandial), bilirubin, GOT, GPT, γ -GT.

Laboratory values in Porphyrias:

	inherited erythropoietic porphyria	acute intermittent porphyria (AIP)	Hereditary coproporphyrin	Porphyria variegata (PV)	porphyria cutanea tarda (PCT)	erythrohep. Protoporphyrin (EPP)
Inheritance	autosomal recessive	dominant	dominant	dominant	dominant	dominant
Forms	erythropoietic	hepatic	hepatic	hepatic	hepatic	erythrohepatic
Photosensitive skin	yes	no	rare	yes	yes	yes
Abdominal pain attacks	no	yes	yes	yes	no	no

<i>Urine</i>						
δ-ALA	n	(+++)	(+++)	(+++)		n
PBG	n	(+++)	(+++)	(+++)	n	n
URO	+++	++	+	+	+++	n
COPRO	++	n	+++	++	+	(+/+++)
<i>Stool</i>						
COPRO	+	n	+++	+	(+)	(+)
PROTO	+	n	+	+++	n	+++
<i>Erythrocytes</i>						
COPRO	+++	n	n	n	n	+

URO	++	n	n	n	n	n
PROTO	(+)	n	n	n	n	+++

n = normal

() = often increased only during a crisis

+ = slightly increased

++ = moderately increased

+++ = significantly increased

ALA = alpha-ALA, delta aminolevulinic acid

PBG = Porphobilinogen

PROTO = Protoporphyrin

URO = Uroporphyrin

COPRO = Coproporphyrin

General:

Examinations if suspecting porphyria:

Urine: δ-aminolevulinic acid, porphobilinogen (PBG) and complete porphyrins. PV (also in latency phase), hereditary coproporphyria, AIP are detected.

Stool: Porphyrins. EPP, latency phases of PV and hereditary coproporphyria are included.

Examinations in diagnosed porphyria: Porphyrins complete in urine, porphyrins differentiated in urine, δ-aminolevulinic acid in urine, porphobilinogen in urine, porphyrins erythrocytic, zinc protoporphyrin erythrocytic, coporphyrin in stool and protoporphyrin in stool.

The following tests are available:

- **Porphyryns, total, in urine**

Material: 10 (20) ml urine

Preanalytics: 24 hour urine, collect light protected, no spontaneous urine, please indicate urine volume.

TAT: 7-10 days*

Method: Photometry

Units: µg/24 h

Ref.- range: <50

- **Porphyrins, total, in stool**

Material: 5 g stool

TAT: 7-10 days*

Method: PHO

Units: $\mu\text{g/g}$ stool

Ref.- range: < 34.0

- **Porphyrins, free in RBC**

Material: 2.7 ml EDTA blood

TAT: 7-10 days*

Method: HPLC

Units: $\mu\text{g/dl}$ Ery.

Ref.- range: < 60.0

- **Delta-aminolevulinic acid, δ -ALA, in urine**

General: Delta-aminolevulinic acid (5-aminolevulinic acid, δ -ALA) is an intermediate product in porphyrin biosynthesis. δ -ALA is generated from succinyl-coenzyme A, glycine and pyridoxal phosphate. Porphobilinogen is formed by condensation of two molecules ALA and catalyzed by the enzyme PBG-synthetase.

Indication: Suspicion of porphyria, lead intoxication

Material: 24 h collection period urine

Preanalytics: 24-hour urine with 10 ml of 10% acetic acid, of which 10 ml should be sent indicating the collected quantity.

TAT: 7-10 days*

Method: RECH

Units: mg/24 h

Ref.- range: <5.0

Note: The combined determination of porphobilinogen, porphyrine and δ -ALA is recommended

- **Porphobilinogen, PBG, in urine**

Material: 20 ml urine

Preanalytics: 24 hour urine, cool and light protected and collected without additives, no spontaneous urine!

TAT: 7-10 days*

Method: RECH

Units: mg/24h

Ref.- range: < 3.0

Note: Porphobilinogen should always be requested together with δ -ALA

- **Uroporphyrins, coproporphyrine, pentacarboxyporphyrin, hexacarboxyporphyrin, heptacarboxyporphyrin in urine**

Material: 10 ml urine

TAT: 7-10 days*

Unit: HPLC

- **Uroporphyrins, coproporphyrine, pentacarboxyporphyrin, hexacarboxyporphyrin, heptacarboxyporphyrin in urine (24 hrs)**

Material: 10 ml urine

TAT: 7-10 days*

Unit: mg/24 hrs.

Note: 24 h urine collection light protected

- **Uroporphyrins, urobilinogen, protoporphyrin, coproporphyrin, pentaporphyrin, hexaporphyrin, heptaporphyrin in stool**

Material: 5 g stool

TAT: 7-10 days*

Method: μ g/g S

Ref. range: see report

- **Zinc protoporphyrin, in RBC**

General :

Zinc protoporphyrin (ZPP) is a compound found in red blood cells when heme production is inhibited by lead and/or by lack of iron. Instead of incorporating a ferrous ion, to form heme, protoporphyrin IX, the immediate precursor of heme, incorporates a zinc ion, forming ZPP. The reaction to insert a ferrous ion into protoporphyrin IX is catalyzed by the enzyme ferrochelatase.

Clinical utility: Measurement of zinc protoporphyrin in red cells has been used as a simple screening test for lead poisoning and for iron deficiency. There are a number of specific clinical situations in which this measurement has been found to be useful. ZPP levels can be **elevated** with lead poisoning, iron deficiency, sickle cell anemia, sideroblastic anemia, anemia of chronic disease, vanadium exposure.

Nevertheless, conflicting reports on the utility and interpretation of ZPP can be found in literature. Data on ZPP findings for acute lead intoxication are limited.

Material: 3 ml EDTA blood

TAT: 7-10 days*

Method: HPLC

Units: $\mu\text{g/g Hb}$

Ref.- range: 0.70 - 4.00

For complete list of laboratory test offered at Freiburg Medical Laboratory, please visit <http://www.fml-dubai.com/parameter-listings/>