Porphyrins

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: 20-40th 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, coproprophyrins and uroporphyrins in erythrocytes increased or normal;

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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;

Secondary Porphyria	
Intoxications	alcohol, chemicals, heavy metals, (esp. lead: ALS and copropor-phyrins in urine, protoporphyrin in urine, stool and in erythrocytes increased);
Liver disorders	cirrhosis, hepatitis, fatty liver, cholestasis, liver changes due to alcohol, porphyrinuria syn-drome, hemochromatosis, medication induced damages;
Blood disorders	hemolytic, medicament 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.

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Laboratory values in Porphyrias:

	inherited erythro-poietic porphyria	acute inter-mittent porphyria (AIP)	Hereditary copro-porphyria	Porphyria variegata (PV)	porphyria cutanea tarda (PCT)	erythrohep. Proto-porphy-ria (EPP)
Inheritance	autosomal recessive	dominant	dominant	dominant	dominant	dominant
Forms	erythropoietic	hepatic	hepatic	hepatic	hepatic	erythro-he-patic
Photosensitive skin	yes	no	rare	yes	yes	yes
Abdominal pain attacks	no	yes	yes	yes	no	no

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

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

- **Porphyrins, 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

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- **Porphyrins, total, in stool**

Material: 5 g stool
TAT: 7-10 days*
Method: PHO
Units: µg/g stool
Ref.- range: < 34.0

- **Porphyrins, free in RBC**

Material: 2.7 ml EDTA blood
TAT: 7-10 days*
Method: HPLC
Units: µg/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

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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: µg/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.

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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:	µg/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/

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