**Quick guide to porphyria testing:**

Porphyria testing can be complex. This is a simplified approach -

* If acute porphyria is suspected or needs to be excluded, request a PBG and urine porphyrins. Contact the laboratory to arrange urgent testing if required. (PBG is a manual test and can only be performed by a small number of scientists)
* If the patient has skin lesions or photosensitivity and/or a history suspicious of acute porphyria, request urine, faeces and whole blood porphyrins and provide a brief history.

Common features of acute porphyria:

Abdominal pain – 97%, Vomiting 85%, Tachycardia – 65%, Hypertension – 64%, Constipation 46%, non-abdominal pain -25%

Background:

* Skin lesions only: PCT is the most common cause, CEP is very rare.
* Either Acute attacks or Skin Lesions : PV (60% skin lesions only, 20% acute attacks only), HCP Acute attacks (almost all with skin lesions all also have acute attacks)
* Acute attacks only - AIP. Worldwide, this is commonest cause of acute porphyria.
* Photosensitivity only(pain, but no blisters with sunlight exposure): EPP

(Skin lesions = blisters, skin fragility, hirsutism)

Porphyrins screening:

* Red Cell Porphyrins

Red cell porphyrins are elevated in EPP and CEP as well as rare homozygous variants of autosomal dominant porphyrias.

The screening test detects both Zn Protoporphyrin and free Protoporphyrins. Zn Protoporphyrin is increased by haemolytic, megaloblastic, sideroblastic anaemias, iron deficiency as well as lead poisoning. Plasma fluorescence will be performed if Red Cell Porphyrin screen is positive.

* PBG

We perform a screening test for PBG. If PBG is positive, the sample is referred for confirmation and quantification.

PBG is always clearly elevated during an acute attack. A negative PBG excludes acute porphyria except for the very rare Doss porphyria. Following recovery from acute porphyria, in VP and HCP, PBG returns to normal within a few days but may remain elevated for months in patients with AIP. Therefore, a positive PBG does not necessarily indicate current acute porphyria; acute porphyria is a clinical diagnosis.

* Urine Porphyrins

Coproporphyrin excretion may be increased by liver disease (cholestatic jaundice, hepatitis and cirrhosis), high alcohol intake or some therapeutic drugs.

Other causes of increased Coproporphyrin excretion include lead toxicity, Dubin-Johnson syndrome, Rotor‘s syndrome and Gilbert’s disease.

If the urine porphyrin screen is positive, the sample is referred for fractionation.

* Faecal Porphyrins

False positive screens may be caused by bacterial metabolism of haem (dietary haem or upper GI bleeding) to porphyrins or by increased dietary intake of porphyrins.

If the faecal porphyrin screen is positive, the sample is referred for fractionation.

* ALA

Testing is not routinely performed, interfering substances commonly causes false elevation as does lead toxicity. ALA is only required if the very rare Doss porphyria is suspected. Contact the laboratory to discuss.

Note that lead can cause false positive porphyrins screens but a blood lead level is the definitive test to assess lead “status”.

**DNA analysis**

Testing is very rarely performed for diagnostic purposes. Mutations are relatively common but penetrance is low. DNA testing is useful in the following settings:

1. Family studies. Most mutations are restricted to a few families. Mutations must first be identified in the family member in whom an acute porphyria has been confirmed unequivocally. Family members can then be screened for the specific mutation.
2. EPP – to identify the pattern of inheritance (recessive or dominant)
3. CEP – Prognosis/severity of disease (C73R mutation)

**Treatment of acute porphyria:**

The treatment is IV Heam and should be initiated as soon as possible. Ideally, discuss treatment with an expert.

Dr Cindy Towns from CCDHB has kindly prepared a protocol for the treatment of acute porphyria.

A separate link to the protocol is available.

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Abbreviations

CEP Congenital Erythropoietic Porphyria

PCT Porphyria Cutanea Tarda

EPP Erythropoietic Protoporphyria

VP Variegate Porphyria

HCP Hereditary Coproporphyria

AIP Acute Intermittent Porphyria

ADP ALA Dehydratase porphyria (Doss porphyria)

PBG Porphobilinogen

ALA ALA

Zn Zinc