Porphyria

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Are a group of rare, inherited disorders of heme biosynthesis, resulting from a deficiency of one of the enzymes on the heme synthetic pathway.

Heme production is impaired, but reduced feedback inhibition of ALA synthase (the rate-limiting step) may maintain adequate heme levels at the expense of overproduction of porphyrins or their precursors

Classification of porphyria

The acute porphyrias:

- PBG synthase deficiency
- Acute intermittent porphyria
- Hereditary coproporphyria
- Variegate porphyria

The cutaneous non-acute porphyrias:

- Porphyria cutanea tarda
- Congenital erythropoietic porphyria
- Protoporphyria

The Acute porphyrias

PBG synthase deficiency

It's an autosomal recessive condition.

PBG concentration is not raised, although that of ALA is, and the condition is very rare.

The other three acute porphyrias are autosomal dominant disorders and have:

- latent phase
- acute phase

- **Latent phase**

Acute intermittent porphyria

It is due to PBG deaminase deficiency , there is increased urinary ALA and PBG excretion, the latent phase is usually asymptomatic.

Hereditary coproporphyria

It is due to coproporphyrinogen oxidase deficiency, there is increased faecal coproporphyrin excretion; the increase in the concentration of porphyrins may produce skin lesions.

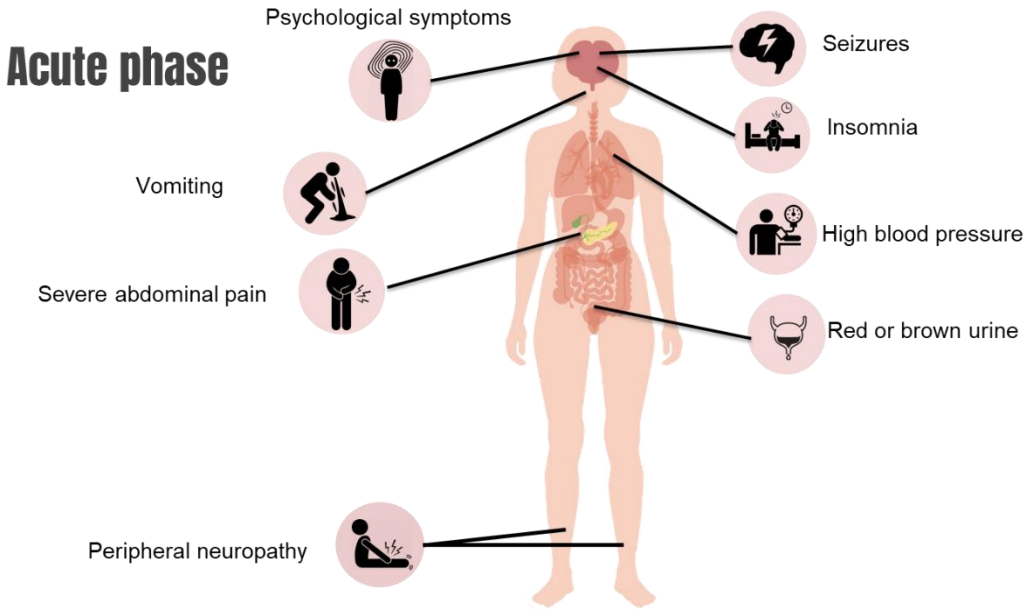
Variegate porphyria

It is due to protoporphyrinogen oxidase deficiency, there is increased faecal protoporphyrin excretion; the increase in the concentration of porphyrins may produce skin lesions.

- **Acute phase**

The life-threatening, acute symptoms that occur in AIP, VP, and HCP are clinically identical.

Acute attacks are more common in woman ,usually occurring first between the ages of 15 and 40 years .



Precipitating factors

Drugs

Alcohol

Menstrual cycle

Stress

Infection

Calorie restriction

Investigations of suspected porphyria

- With the exception of PBG synthase deficiency (in which case ALA concentration would be expected to be raised) , attacks of acute porphyria are associated with an elevated urinary excretion of PBG.
- PBG may spontaneously oxidize to form uroporphyrin when exposed to air and light.
- Fresh random urine specimen, protected from light, should be sent to the laboratory for the quantitation of PBG .
- If an acute porphyria is confirmed, the concentration of porphyrins in urine and faeces should be measured.
- A negative result excludes an acute porphyria provided the patient is symptomatic at the time of sample collection. In between acute attacks, the excretion of PBG may return to normal.

Treatment of acute porphyria

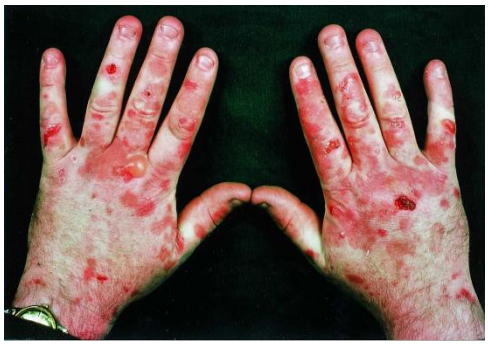
Heme arginate, given by slow intravenous infusion, can result in a reduction in ALA and PBG concentrations and thus reduce some of the features of the acute attack.

The cutaneous non-acute porphyrias

Porphyria cutanea tarda

This is the most common porphyria.

In patients with PCT, the skin is sensitive to minor trauma, particularly in sun-exposed areas; the most common presenting feature is blistering on the backs of the hands.



Less commonly, the lesions appear on the face. Increased facial hair and hyperpigmentation. Acute attacks do not occur, but this type of porphyria is associated with hepatic damage.

- The basic defect is an inability to convert uroporphyrinogen to coproporphyrinogen due to a deficiency of uroporphyrinogen decarboxylase.
- The impaired conversion leads to an accumulation uroporphyrinogen and porphyrins intermediate between it and coproporphyrinogen. These deposit in the skin and are excreted in the urine in increased amounts.

Erythropoietic porphyrias

Two rare inherited disorders are associated with the accumulation of porphyrins in erythrocytes. Acute porphyric attacks do not occur and ALA and PBG excretion are normal.

Congenital erythropoietic porphyria

- Is inherited as an autosomal recessive characteristic due to uroporphyrinogen III synthase deficiency.
- blood erythrocyte and plasma uroporphyrin I concentrations are very high from infancy onwards and there is severe photosensitivity.
- Porphyrins are also deposited in bones and teeth, the teeth may be brownish-pink in colour.
- Hirsutism, especially of the face, also occurs and there is haemolytic anaemia.
- Urinary porphyrin concentrations are grossly increased, although faecal porphyrin levels are less so.

Protoporphyria

- This is an autosomal dominant disorder due to ferrochelatase deficiency in which protoporphyrin concentrations are increased in erythrocytes and faeces. There is mild photosensitivity, and hepatocellular damage may lead to liver failure.

Investigations of cutaneous non acute porphyria

- Increased concentrations of erythrocyte porphyrins suggest protoporphyria or congenital erythropoietic porphyria.
- Increased concentrations of urinary porphyrins suggest porphyria cutanea tarda or congenital erythropoietic porphyria.
- Increased concentrations of faecal porphyrins occur in protoporphyria.

Treatment

- Porphyria cutanea tarda, venesection may be used to reduce iron stores and or
- The erythropoietic porphyrias can be treated by sunlight avoidance,