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Variegate porphyria

What is variegate porphyria?

Variegate porphyria is a subtype of porphyria. It is an inherited disorder characterised by skin [photosensitivity](#) (reaction to light), systemic symptoms arising from neurological problems, or both. It is considered very uncommon or rare throughout the world apart from in South Africa, where it is estimated that 1 in 300 of South Africa's white population is affected. This gene mutation is traceable to Dutch immigrants who married there in 1680.

What causes variegate porphyria?

Variegate porphyria is caused by a gene mutation of the protoporphyrinogen oxidase enzyme protein (PPOX). This enzyme is critical in the chemical process that leads to haem production. Haem is the red pigment in blood cells and is an important component of haemoglobin, the molecule that carries oxygen in the blood. In people with variegate porphyria activity of the PPOX enzyme is reduced by 50%. This means there is a build-up of toxic porphyrins particularly uroporphyrin and coproporphyrin, which leads to blistering.

Variegate porphyria is an autosomal dominant disorder. This means that a male or female carrying the gene will pass it on to half of his or her children.

In most people with variegate porphyria signs and symptoms may only become apparent when they are exposed to non-genetic factors such as certain drugs, stress, dieting or fasting, and certain hormones. These factors increase the demand for haem and the enzymes to make haem. The combinations of increased demand and reduced activity of PPOX disrupts haem production and triggers an acute variegate porphyria attack.

What are the signs and symptoms of variegate porphyria?

Approximately 60% of patients with a PPOX gene mutation will experience no symptoms. In those that are symptomatic, skin photosensitivity occurs 3–5 times more often than systemic symptoms arising from neurological dysfunction. In a few cases, both skin and systemic symptoms occur together. In most cases acute attacks usually begin in adulthood and can often be linked to history of a new medication.

Signs and symptoms of variegate porphyria rarely occur in childhood, however in cases where it does occur it is usually more severe and even debilitating. Children with this condition may have mental retardation and grow more slowly.

Variegate porphyria



Skin photosensitivity

Most people with variegate porphyria have skin that is overly sensitive to sunlight. Areas exposed to the sun often develop blistering, scarring, changes in skin colour and increased hair growth.

Systemic symptoms

Acute attacks cause severe abdominal pain, uncontrolled vomiting, diarrhoea and constipation. Neurological manifestations include muscle and limb weakness that may progress to areflexic quadriparesis (weak arms and legs), seizures, and mental changes such as anxiety and hallucinations. Other symptoms include changes in heart rate and blood pressure, and respiratory distress. Electrolyte imbalance such as low sodium and magnesium levels may be present.

Investigations

During acute attacks, the diagnosis of variegate porphyria is confirmed by:

- High levels of urinary porphyrins (aminolevulinic acid, porphobilinogen, coproporphyrin and to a lesser extent, uroporphyrin). Between attacks, urine results may be normal.
- High levels of faecal porphyrins (coproporphyrin, protoporphyrin and porphyrin X)
- Plasma fluorescence shows a peak at 625–7 nm in symptomatic and many asymptomatic carriers

These tests should be done by an experienced and quality-assured laboratory as precision is critical.

There is a rapid test kit to identify elevated porphobilinogen if required in an emergency.

The features of a [skin biopsy](#) may appear similar to porphyria cutanea tarda. The blister is due to clefting under the epidermis and is not associated with much inflammation. Blood vessel walls and basement membranes are thickened.

Other tests will depend on the general health of the individual and symptoms.

How is variegate porphyria treated?

The management of an acute attack of variegate porphyria is the same as for acute attacks of all other porphyria disorders. Management of acute attacks consists of the following:

- Manage fluid and electrolyte imbalances
- Control seizures with benzodiazepines, magnesium sulphate or [gabapentin](#)
- Control severe tachycardia and hypertension with beta blockers
- Manage severe pain with opioid analgesics
- Reduce nausea and vomiting with phenothiazines
- Administer IV haem-analogue, particularly in severe cases that are not responsive to symptomatic management, fluids and carbohydrates within a day.

Patients with variegate porphyria must be informed about the factors that can trigger the acute symptoms of the condition. Whilst most triggers of variegate porphyria appear to be drugs, in some cases the inducing factor is unknown. Hence it is sensible to minimize exposure to risk factors. Patients should adhere to the following management points as much as possible.

- Avoid carbohydrate-restricted diets; glucose in food or drink may stop an attack.
- Moderate alcohol intake (it is best to avoid alcohol altogether) and stop smoking
- Institute any necessary hormonal therapy with caution
- Apply an opaque [sun-block](#) such as those containing zinc or titanium dioxide and cover up when outside; the responsible light is the "Soret" band at 400 nm which is unfortunately not blocked by most sunscreens
- Use tanning cream containing dihydroxyacetone: this can block the responsible light to some extent.

It can be difficult to determine which drugs should be avoided by people with variegate porphyria, and tolerance of these can vary between patients. Mimimise drug use and refer to a list of safe and unsafe drugs (see links to other websites below).

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Related information

References:

- Book: Textbook of Dermatology. Ed Rook A, Wilkinson DS, Ebling FJB, Champion RH, Burton JL. Fourth edition. Blackwell Scientific Publications.
- [Patient's and Doctor's Guide to Medication in Acute Porphyria](#) PDF file: Canadian Porphyria Foundation

On DermNet NZ:

- [Porphyria cutanea tarda](#)
- [Photosensitivity](#)

Other websites:

- [Variegate Porphyria](#) - from emedicine dermatology, the online textbook
- [The Drug Database of Acute Porphyria](#) Norwegian Porphyria Centre (NAPOS)
- [American Porphyria Foundation](#)
- [Canadian Porphyria Foundation](#)

Books about skin diseases:

See the [DermNet NZ bookstore](#)

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DermNet does not provide an on-line consultation service.

If you have any concerns with your skin or its treatment, see a [dermatologist](#) for advice.

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