WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 17, 1373-1381. Review Article ISSN 2277– 7105

PORPHYRIA

Mandar Chavan*, Rahul Chaurasiya, Vikas Gupta and Abhishek Dubey

India.

Article Received on
14 August 2018,

Revised on 05 Sept. 2018,
Accepted on 26 Sept. 2018,

DOI: 10.20959/wjpr201817-13455

***Corresponding Author**
Mandar Chavan
India.

Porphyria

What Is Porphyria?

The terms *porphyrin* and *porphyria* are derived from the Greek word *porphyrus*, meaning purple. Urine from some porphyria patients may be reddish in colour due to the presence of excess porphyrins and related substances in the urine, and the urine may darken after exposure to light.

Porphyria is a group of 7 inherited metabolic disorders (diseases), caused by 7 different faulty genes. They cannot be “caught” like a cold. Metabolic means they affect the chemistry of the body, not its structure. The 7 genes all slow the production of haem (used in haemoglobin and other body chemicals which transfer oxygen). Because the cause is in a gene, there may be several people in a family who have inherited it. Many of these will have no problems. All

seven are rare. Two are so rare that even some experts have not seen them. This can make diagnosis difficult.[1]

Porphyria is a group of diseases in which substances called porphyrins build up, negatively affecting the skin or nervous system.The frequency of porphyria is unclear. It is estimated that it affects 1 to 100 per 50,000 people. Rates vary around the world.Porphyria cutanea tarda is believed to be the most common type.The disease was described at least as early as 370 BC by Hippocrates.[2]

Most types of porphyria are inherited from a person's parents and are due to a mutation in one of the genes that make heme.They may be inherited in an autosomal dominant, autosomal recessive, or X-linked dominant manner. One type, porphyria cutanea tarda, may also be due to increased iron in the liver, hepatitis C, alcohol, or HIV/AIDS. The underlying mechanism results in a decrease in the amount of heme produced and a build-up of substances involved in making heme. Porphyrias may also be classified by whether the liver or the bone marrow is affected. Diagnosis is typically by blood, urine, and stool tests. Genetic testing may be done to determine the specific mutation.[2]

The exact rates of porphyria are unknown and vary around the world. For example, porphyria cutanea tarda is most common in the United States, and variegate porphyria is most common in South America.[3]

What are the types of porphyria?

Each of the eight types of porphyria corresponds to low levels of a specific enzyme in the heme biosynthetic pathway. Experts often classify porphyrias as acute or cutaneous based on the symptoms a person experiences:

- Acute porphyrias affect the nervous system. They occur rapidly and last only a short time.
- Cutaneous porphyrias affect the skin.

  Two types of acute porphyrias, hereditary coproporphyria and variegate porphyria, can also have cutaneous symptoms.

  Experts also classify porphyrias as erythropoietic or hepatic:
- In erythropoietic porphyrias, the body overproduces porphyrins, mainly in the bone marrow.
- In hepatic porphyrias, the body overproduces porphyrins and porphyrin precursors, mainly in the liver.[3]

Type of Porphyria	Deficient Enzyme
delta-aminolevulinate-dehydratase deficiency porphyria	delta-aminolevulinic acid dehydratase
acute intermittent porphyria	porphobilinogen deaminase
hereditary coproporphyria	coproporphyrinogen oxidase
variegate porphyria	protoporphyrinogen oxidase
congenital erythropoietic porphyria	uroporphyrinogen III cosynthase
porphyria cutanea tarda	uroporphyrinogen decarboxylase (~75% deficiency)
hepatoerythropoietic porphyria	uroporphyrinogen decarboxylase (~90% deficiency)
erythropoietic protoporphyria*	ferrochelatase (~75% deficiency)

Acute Intermittent Porphyria (AIP)

This form of porphyria is perhaps the most severe of all of the porphyric syndromes in terms of its symptomatology. It is inherited in an autosomal dominant fashion and is slightly more common in females than in males. There are several mutations of a single gene, located on chromosome 11, which controls the activity of the enzyme porphobilinogen deaminase (PGB.D). This enzyme is responsible for the joining of 4 porphobilinogen molecules into a linear chain to form a compound called hydroxymethylbilane which is then converted into the cyclic or ring structure characteristic of the porphyrin molecule. The intracellular activity of the enzyme PGB.D in patients with AIP is decreased, usually to less than 50% in both red blood cells and liver cells.[4]

Occasionally the patients themselves note that their urine turns reddish brown a day or so before the onset of their symptoms and clears as they get better.

Frequently the acute attacks disappear with little medical intervention but occasionally the patient has to be hospitalized.[4]

The cutaneous (skin) porphyrias

It can all give sensitivity to sunlight on exposed areas of skin. As with all porphyrias, the severity of the problem varies enormously. Sunlight should be avoided as much as possible. When avoiding sunlight is not possible, special sunblocks which block violet light can help. (In mild cases, high-factor sun cream with high-UVA protection may be enough.) Hats and clothing which cover up the skin are also recommended. See our skin safety page for more information.

Cutaneous porphyrias comprise:

Porphyria Cutanea Tarda (PCT)

Erythropoietic Protoporphyria (EPP)

X-Linked Dominant Erythropoietic Protoporphyria (XLDPP)[5]

The cutaneous porphyrias are all accompanied by elevated total plasma porphyrins, and are specifically diagnosed by measurements of porphyrins in RBCs, plasma, urine, and stool, as well as by genetic or enzyme analysis. Treatment involves avoidance of sunlight, measures to protect the skin, and sometimes other treatments directed according to the specific diagnosis.[6] [7]

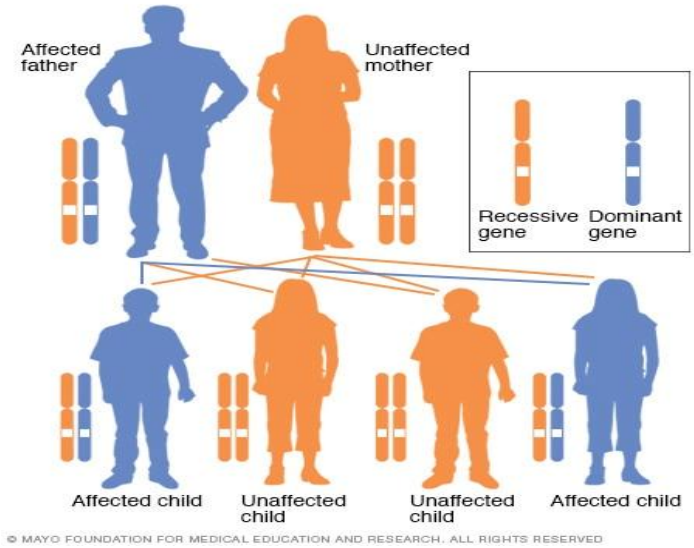

Figure 1: autosomal dominant inheritance pattern.

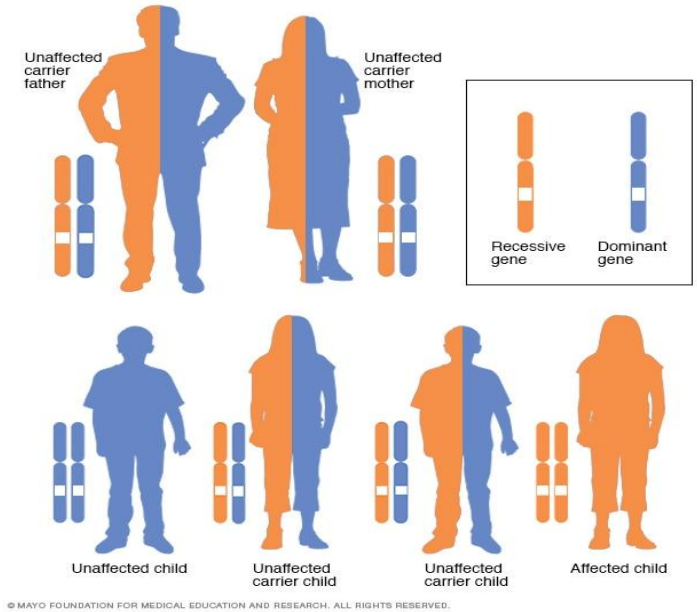

Figure 2: Autosomal recessive inheritance pattern.

Causes

All types of porphyria involve a problem in the production of heme. Heme is a component of hemoglobin, the protein in red blood cells that carries oxygen from your lungs to all parts of your body. Heme production, which occurs in the bone marrow and liver, involves eight different enzymes — a shortage (deficiency) of a specific enzyme determines the type of porphyria.

- In cutaneous porphyria, the porphyrins build up in the skin, and when exposed to sunlight, cause symptoms. In acute porphyrias, the buildup damages the nervous system
  Genetic forms
  Most forms of porphyria are inherited. Porphyria can occur if you inherit:
- A defective gene from one of your parents (autosomal dominant pattern)
- Defective genes from both parent (autosomal recessive pattern)

Just because you inherit a gene or genes that can cause porphyria doesn't mean that you'll have signs and symptoms. You might have what's called latent porphyria, and never have symptoms. This is the case for most carriers of the abnormal genes.

Acquired forms

Porphyria cutanea tarda (PCT) typically is acquired rather than inherited, although the enzyme deficiency may be inherited. Certain triggers that impact enzyme production — such as too much iron in the body, liver disease, estrogen medication, smoking or excessive alcohol use — can cause symptoms.[8]

Symptoms

Symptoms of porphyria can vary widely in severity, by type and among individuals. Some people with the gene mutations that cause porphyria never have any symptoms.

Acute porphyrias

Acute porphyrias include forms of the disease that typically cause nervous system symptoms, which appear quickly and can be severe. Symptoms may last days to weeks and usually improve slowly after the attack. Acute intermittent porphyria is the common form of acute porphyria.

Signs and symptoms of acute porphyria may include:

- Severe abdominal pain

- Pain in your chest, legs or back
- Constipation or diarrhea
- Nausea and vomiting
- Muscle pain, tingling, numbness, weakness or paralysis
- Red or brown urine
- Mental changes, such as anxiety, confusion, hallucinations, disorientation or paranoia
- Breathing problems
- Urination problems
- Rapid or irregular heartbeats you can feel (palpitations)
- High blood pressure
- Seizures.[8]

Long-term complications in some patients have included:

Chronic pain

- Depression
- Kidney damage
- Liver cancer.[9]

Cutaneous porphyrias

Cutaneous porphyrias include forms of the disease that cause skin symptoms as a result of sensitivity to sunlight, but these forms don't usually affect your nervous system. Porphyria cutanea tarda (PCT) is the most common type of all the porphyrias.

As a result of sun exposure, you may experience:

- Sensitivity to the sun and sometimes artificial light, causing burning pain
- Sudden painful skin redness (erythema) and swelling (edema
- Blisters on exposed skin, usually the hands, arms and face
- Fragile thin skin with changes in skin colour (pigment)
- Itching
- Excessive hair growth in affected areas
- Red or brown urine.[8]

Diagnosis

Many signs and symptoms of porphyria are similar to those of other more common diseases. Also, because porphyria is rare, it can be more difficult to diagnose.

Lab tests are required to make a definitive diagnosis of porphyria and to determine which form of the disease you have. Different tests are performed depending on the type of porphyria your doctor suspects. Tests include a combination of blood, urine or stool testing.

More tests may be needed to confirm the type of porphyria you have. Genetic testing and counseling may be recommended in the family of a person with porphyria.[8]

Many tests can help diagnose this condition.

Tests that look for physical problems include:

- computed tomography (CT) scans
- chest X-ray
- echocardiogram (EKG)

Tests for blood problems include:

- urine test for fluorescence
- porphobilinogen (PBG) urine test
- complete blood count (CBC).[10]

Treatment

Treatment depends on the type of porphyria you have and the severity of symptoms. Treatment includes identifying and avoiding symptom triggers and then relieving symptoms when they occur.

Avoiding triggers

Avoiding triggers may include:

- Not using medications known to trigger acute attacks. Ask your doctor for a list of safe and unsafe drugs.
- Not using alcohol or recreational drugs.
- Avoiding fasting and dieting that involves severe calorie restriction.
- Not smoking.
- Taking certain hormones to prevent premenstrual attacks.
- Minimizing sun exposure. When you're outdoors, wear protective clothing, and use an opaque blocking sunscreen, such as one with zinc oxide. When indoors, use window filters.
- Treating infections and other illnesses promptly.

- Taking steps to reduce emotional stress.

Acute porphyrias

Treatment of acute porphyria attacks focuses on providing rapid treatment of symptoms and preventing complications. Treatment may include:

- Injections of hemin, a medication that is a form of heme, to limit the body's production of porphyrins
- Intravenous sugar (glucose), or sugar taken by mouth, if able, to maintain an adequate intake of carbohydrates
- Hospitalization for treatment of symptoms, such as severe pain, vomiting, dehydration or problems breathing

Cutaneous porphyrias

Treatment of cutaneous porphyrias focuses on reducing exposure to triggers such as sunlight and reducing the amount of porphyrins in your body to help eliminate your symptoms. This may include:

- Periodically drawing blood (phlebotomy) to reduce the iron in your body, which decreases porphyrins.
- Taking a drug used to treat malaria — hydroxychloroquine (Plaquenil) or, less often, chloroquine (Aralen) — to absorb excess porphyrins and help your body get rid of them more quickly than usual. These medications are generally used only in people who can't tolerate a phlebotomy.
- A dietary supplement to replace vitamin D deficiency caused by avoidance of sunlight.[9]

Prevention

Porphyria cannot be prevented. However, symptoms can be reduced by avoiding or eliminating triggers.

Factors that should be eliminated include:

- recreational drugs
- mental stress
- excessive drinking
- certain antibiotics

Preventing erythropoietic symptoms focuses on reducing light exposure by:

- staying out of bright sunlight

- wearing long sleeves, hats, and other protective clothing while outside
- Asking for protection during surgery – in rare cases phototoxic injury can occur. This happens when light perforates the organs and leads to infection.[10]

REFERENCE'S

1. www.porphyriyafoundation.org.uk
2. https://enWikipedia.org
3. https://www.niddk.nin.gov
4. https://www.medicinenet.com
5. https://albertaporphyriasociety.weebly.com
6. https://www.porphyria.org.uk
7. https://www.merckmanuals.com
8. https://www.mayoclinic.org
9. www.webmd.com
10. https://www.healthline.com