CONDITION

Mixed hepatic porphyria

Mixed hepatic porphyria is an inherited condition that can cause acute nerve-related attacks and light-sensitive skin symptoms.

WHAT IT IS
Inherited porphyria causing nerve attacks and light-sensitive skin

BODY SYSTEM
Liver, nervous system, and skin

MAIN SYMPTOMS
Abdominal pain, nausea, weakness, blistering sun-exposed skin

WHAT CAUSES IT
Inherited PPOX gene change affecting haem production

HOW IT IS DIAGNOSED
Urine PBG, plasma and stool porphyrins, PPOX genetic testing

MAIN TREATMENT
Trigger avoidance, attack treatment, skin protection, specialist monitoring

CAN IT BE CURED?
No - the inherited change remains

IS IT AN EMERGENCY?
Sometimes - severe pain, weakness, confusion, or breathing trouble

LONG-TERM OUTLOOK
Many remain well with trigger avoidance and specialist care

Overview

Mixed hepatic porphyria is an older name commonly used for variegate porphyria . "Hepatic" means related to the liver. "Mixed" refers to its ability to cause two different groups of symptoms: sudden attacks involving the nervous system and symptoms affecting sun-exposed skin.

The condition is one of the acute hepatic porphyrias . These are inherited conditions that affect the body's production of haem, a substance needed for haemoglobin and many enzymes. Haemoglobin carries oxygen in the blood.

Haem is made through a series of chemical steps. In mixed hepatic porphyria, one of these steps does not work normally. This can allow chemicals called porphyrin precursors and porphyrins to build up. The precursors are linked to acute nerve-related attacks, while

porphyrins in the skin react with light and can cause skin damage.

Many people who inherit the genetic change never have symptoms. Others have skin symptoms, acute attacks, or both. Because "mixed hepatic porphyria" is not always used consistently, laboratory and genetic results are important for confirming the exact type.

Symptoms

Symptoms usually fall into two groups. A person may experience either group without the other.

An acute attack develops over hours or days. It can cause:

Abdominal pain is common during an attack, but it does not always come with tenderness or swelling. Symptoms can resemble many more common conditions, so symptoms alone cannot confirm porphyria.

A severe attack can affect the nerves controlling movement and breathing. Seizures may occur, sometimes alongside a low blood sodium level. These complications need hospital treatment.

Skin symptoms occur mainly on areas exposed to sunlight, especially the backs of the hands, forearms, face, and neck. They may include:

The skin reaction is usually caused by visible light as well as ultraviolet light. It is not the same as an ordinary sunburn and may not start immediately after exposure.

- Severe, persistent abdominal pain without an obvious physical cause
- Nausea, vomiting, constipation, or sometimes diarrhoea
- Pain in the back, chest, arms, or legs
- Fast heartbeat or raised blood pressure
- Anxiety, agitation, confusion, or difficulty sleeping
- Muscle weakness, tingling, or numbness
- Dark or reddish urine, especially after it stands in light
- Fragile skin that tears easily
- Blisters after light exposure or minor knocks
- Slow-healing sores and small scars
- Tiny white bumps called milia

- Changes in skin colour

Causes and risk factors

Mixed hepatic porphyria is usually caused by a change in the PPOX gene . This gene provides instructions for an enzyme involved in making haem.

The genetic change is inherited in an autosomal dominant pattern. This means a person with the change has a 1 in 2 chance of passing it to each child. Inheriting it does not mean symptoms will definitely develop.

Acute attacks are more likely when the liver increases haem production. Possible triggers include:

Not every suspected trigger affects every person. Medicines are especially important because some are considered unsafe in acute porphyria, while many common medicines are safe. A specialist porphyria medicines database can be used to check them.

Sunlight and other strong visible-light sources can trigger skin damage. Ordinary window glass may not block all relevant light.

- Certain medicines
- Fasting, crash dieting, or a very low calorie intake
- Hormonal changes, including menstrual hormone changes
- Alcohol
- Smoking
- Infections, surgery, or major physical stress

Diagnosis

Testing is most informative during symptoms. When an acute attack is suspected, the main first test is usually a fresh urine sample for porphobilinogen , often shortened to PBG, and aminolevulinic acid , or ALA. These porphyrin precursors are usually substantially raised during an acute attack.

A normal PBG result during current, significant symptoms makes an acute porphyria attack much less likely, although testing and sample handling must be appropriate.

Further tests identify the specific type of porphyria. These may include:

PBG can return toward normal between attacks. Plasma and stool porphyrin tests may

therefore be particularly useful when mixed hepatic porphyria is suspected outside an acute attack.

Genetic testing can confirm the inherited change after biochemical tests support the diagnosis. It can also allow adult relatives to have targeted testing for the same family change. Genetic counselling can help people understand the results and what they may mean for relatives or future children.

- Porphyrin measurements in blood plasma, urine, and stool
- A plasma fluorescence scan, which examines how porphyrins respond to light
- Stool testing for a characteristic porphyrin pattern
- Genetic testing for a harmful change in the PPOX gene

Treatment and management

Treatment has three aims: controlling an acute attack, reducing future attacks, and protecting the skin.

A suspected acute attack is assessed promptly. Hospital care may include monitoring of breathing, muscle strength, heart rate, blood pressure, kidney function, and blood sodium. Treatment can also address pain, nausea, vomiting, and other symptoms using medicines considered safe for acute porphyria.

Intravenous hemin reduces the liver's production of harmful porphyrin precursors and is the main specific treatment for a significant acute attack. It is given through a vein under medical supervision. Carbohydrate treatment may be considered in selected mild situations, but it is not a substitute for urgent assessment of severe or worsening symptoms.

A medicine that reduces production of an early haem-making enzyme may be considered for some people with recurrent acute hepatic porphyria attacks. This treatment requires specialist assessment and ongoing monitoring. It is not needed by everyone who carries the genetic change.

Managing skin symptoms focuses on reducing exposure to the wavelengths of light that activate porphyrins. Helpful measures may include:

Standard sunscreens mainly block ultraviolet light and may not fully prevent porphyria-related skin injury.

Long-term management often includes a written attack plan, a checked list of medicines, and follow-up with a porphyria or metabolic specialist. Do not stop a prescribed medicine suddenly because of a porphyria warning; it should first be checked with the prescriber or a specialist

medicines service.

- Covering the hands, arms, face, and neck with suitable clothing
- Wearing gloves and a broad-brimmed hat outdoors
- Using opaque or visible-light-blocking skin products
- Protecting fragile skin from friction and minor injuries
- Keeping blisters and wounds clean and seeking care if they become infected

Complications

Most people do not develop every possible complication. During a severe attack, complications can include:

Nerve recovery can be slow after a severe attack. Weakness may improve over weeks or months, although recovery is not always complete.

Repeated attacks may be associated with chronic pain, reduced kidney function, and high blood pressure. Acute hepatic porphyrias are also linked to an increased risk of primary liver cancer. Specialist follow-up may therefore include blood pressure, kidney, and liver checks, with liver surveillance based on age, personal risk, and local guidance.

Repeated skin injury can lead to scarring, changes in skin colour, or infection.

- Low blood sodium
- Seizures
- Significant muscle weakness or paralysis
- Breathing muscle weakness
- Abnormal heart rate or blood pressure
- Dehydration or kidney problems

Prevention

The inherited genetic change cannot currently be prevented or removed. However, many acute attacks and skin injuries may be preventable.

A porphyria specialist can help identify triggers that are relevant to you. This often includes checking medicines before they are started, avoiding prolonged fasting or crash diets, limiting or avoiding alcohol, and not smoking.

Regular meals and adequate carbohydrate intake are generally important, but mixed hepatic porphyria does not require everyone to follow the same special diet. Weight loss, if planned, should be gradual and discussed with a clinician familiar with acute porphyria.

Covering sun-exposed skin can reduce blistering and repeated damage. Since visible light is involved, protective clothing and opaque barriers may work better than relying on ordinary sunscreen alone.

Relatives who carry the family PPOX change may benefit from learning about medicine safety and attack triggers even if they have never had symptoms. Testing cannot prevent inheritance, but it can help with informed health and family-planning decisions.

Living with it and what to expect

The course differs from person to person. Many people with the genetic change remain well throughout life. Some mainly have skin fragility, while others have one or more acute attacks. A smaller group experiences recurrent attacks.

Between acute attacks, porphyria-related abdominal and nerve symptoms may disappear completely. After a severe attack, weakness, fatigue, pain, or reduced stamina can continue for months. Rehabilitation or physiotherapy may be needed when movement has been affected.

Skin sensitivity may continue even when there are no acute attacks. Consistent light protection can reduce new injuries, but existing scars may remain.

Hormonal changes, illness, surgery, and new medicines can alter attack risk over time. Planning ahead is useful before surgery, pregnancy, or a major change in medication. Anaesthesia can be given safely when the team knows about the condition and checks each medicine.

Keeping an emergency information card or digital record can help unfamiliar healthcare teams find the correct tests and medicine-safety information. Routine follow-up may include reviewing attacks and triggers, checking blood pressure and kidney and liver health, and discussing the emotional effect of living with an unpredictable condition.

When to get medical help

Seek emergency medical care for possible acute porphyria symptoms when there is:

Tell the emergency team about the porphyria diagnosis or family history. Acute testing should ideally include urine PBG and ALA before specific treatment, but necessary care should not be delayed.

Arrange prompt, non-emergency medical advice for new blistering, wounds that are not healing, signs of skin infection, repeated milder abdominal episodes, or possible medicine-related symptoms.

Routine specialist follow-up is appropriate when you are well. It can be used to review medicine safety, skin protection, family testing, attack planning, and recommended kidney and liver monitoring.

- Severe or rapidly worsening abdominal pain
- New muscle weakness, trouble walking, or difficulty lifting the limbs
- Trouble breathing or swallowing
- A seizure, collapse, marked confusion, or unusual drowsiness
- Repeated vomiting with difficulty keeping fluids down
- Severe symptoms in someone known to have an acute hepatic porphyria

Common questions

Is mixed hepatic porphyria the same as variegate porphyria?

The term is most commonly used for variegate porphyria because that condition can cause both acute nerve-related attacks and skin symptoms. However, older records may use porphyria names inconsistently. Biochemical and genetic results can clarify the exact type.

Can I have the gene without having symptoms?

Yes. Many people with a PPOX gene change never develop an acute attack or noticeable skin symptoms. They can still pass the change to their children and should know about medicines and situations that may trigger an attack.

Can mixed hepatic porphyria be cured?

There is no routine treatment that removes the inherited change. Symptoms and attack risk can often be managed. Liver transplantation can stop the liver-related biochemical problem in exceptional, severe cases, but it is major surgery and is not a standard treatment for most people.

Will sunlight always cause blisters?

Not necessarily. Light sensitivity differs between people and can change over time. The total amount of light exposure and protection used both matter. Visible light can be involved, so ordinary sunscreen may not provide enough protection by itself.

Is dark urine proof of an attack?

No. Urine may darken because porphyrin-related chemicals change after exposure to light, but many other conditions can also change urine colour. An acute attack is confirmed with laboratory testing, particularly urine PBG and ALA collected during symptoms.

Can I take ordinary medicines?

Many medicines are safe, but some can trigger an acute attack. Each medicine, including hormonal treatments and non-prescription products, should be checked in a recognised porphyria medicines database. A needed medicine should not be stopped suddenly without medical advice.

Sources

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