Porphyria
Porphyria

The British Liver Trust works to:
● support people with all kinds of liver disease
● improve knowledge and understanding of the liver and related health issues
● encourage and fund research into new treatments
● lobby for better services.

All our publications are reviewed by medical specialists and people living with liver disease. Our website provides information on all forms of adult liver disease and our Helpline gives advice and support on general and medical enquiries. Call us on 0800 652 7330 or visit www.britishlivertrust.org.uk

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The liver

Your liver is your body’s ‘factory’ carrying out hundreds of jobs that are vital to life. It is very tough and able to continue to function when most of it is damaged. It can also repair itself – even renewing large sections.

Your liver has around 500 different functions. Importantly it:
● fights infections and disease
● destroys and deals with poisons and drugs
● filters and cleans the blood
● controls the amount of cholesterol
● produces and maintains the balance of hormones
● produces chemicals – enzymes and other proteins – responsible for most of the chemical reactions in the body, for example, blood clotting and repairing tissue
● processes food once it has been digested
● produces bile to help break down food in the gut
● stores energy that can be used rapidly when the body needs it most
● stores sugars, vitamins and minerals, including iron
● repairs damage and renews itself.

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How liver disease develops

Liver damage develops over time. Any inflammation of the liver is known as hepatitis, whatever its cause. Sudden inflammation of the liver is known as acute hepatitis. Where inflammation of the liver lasts longer than six months the condition is known as chronic hepatitis.

Fibrosis is where scar tissue is formed in the inflamed liver. Fibrosis can take a variable time to develop. Although scar tissue is present the liver keeps on functioning quite well. Treating the cause of the inflammation may prevent the formation of further liver damage and may stop or reverse some or all of the scarring.

Cirrhosis is when inflammation and fibrosis has spread throughout the liver and disrupts the shape and function of the liver. Even at this stage, people can have no signs or symptoms of liver disease. When the working capacity of liver cells has been badly impaired and they are unable to repair or renew the liver, permanent damage occurs.

Cirrhosis can lead to liver failure or liver cancer. All the chemicals and waste products that the liver has to deal with build up in the body. The liver is now so damaged that the whole body becomes poisoned by the waste products and this stage is known as end stage liver disease. In the final stages of liver disease the building up of waste products may cause multiple organ failure and lead to death.
What is porphyria?

Porphyria is the name given a group of very rare metabolic disorders that occur when your body is unable to produce enough of a substance called haem.

Haem is required for many bodily functions. It is a component of haemoglobin, a vital protein which helps transport oxygen around your body and the pigment that gives red blood cells their colour. Haem also helps to form many other important proteins and is found in all body tissues, but mostly in red blood cells, bone marrow and the liver.

To produce haem, your body needs to convert two simple substances, aminolaevulinate acid (ALA) and porphobilinogen (PBG), known as porphyrin precursors, into more complicated substances called porphyrins. These are then converted from one type of porphyrin into another to form, haem.

The steps in this process, or ‘pathway’, are carried out by seven specialised proteins known as enzymes. If you inherit or develop a defect (usually termed a ‘deficiency’) in these enzymes, the process may not work properly and can cause porphyrins to build up in your body.

This accumulation can either affect the nervous system to provoke ‘acute attacks’ of physical pain or cause damage to your skin – sometimes both.

It can also cause a person’s urine to turn a reddish-purple colour. In fact, the terms ‘porphyrin’ and ‘porphyria’ stem from the Greek word for purple, ‘porphyrus’.

The symptoms you have will depend on which enzyme is affected. There are more than seven types of porphyria, each categorised according to the particular enzyme deficiency and the symptoms associated with it.

Because of this it is difficult to talk about porphyria in general terms. It is possible to divide the disorders into those that mostly affect the brain, known as acute porphyrias, and those that cause skin problems, called cutaneous porphyrias. ‘Cutaneous’ means relating to the skin; disorders that share the characteristics of both are called neurocutaneous porphyrias.

Acute porphyrias are acute intermittent porphyria (AIP), the most common form in the UK and the most severe, and aminolevulinate dehydratase deficiency porphyria (ADP). This form is similar to AIP but extremely rare.

Cutaneous porphyrias are porphyria cutanea tarda (PCT), the most common of the skin disorders and the most common globally; erythropoietic porphyria (EPP), a very uncommon form that causes symptoms very early in life; and the rarest form, congenital erythropoietic porphyria (CEP), which also occurs early.

Porphyrias causing both acute and cutaneous disorders are hereditary coproporphyria (HCP) and variegate porphyria (VP).
Porphyria can appear in childhood, as seen in erythropoietic porphyria (EPP), but the onset is usually between the ages of 20 and 40 and affects women more than men.

Acute forms can cause serious damage to your liver and kidneys. In some severe cases, people may need a liver transplant. Attacks or seizures can lead to complications such as respiratory failure which can be fatal if not treated. Around 1% of acute attacks of porphyria are fatal.

It is important that the type of porphyria you have is diagnosed as soon as possible. With good management, severe symptoms can be avoided and most people with porphyria (‘porphyriacs’) do in fact lead relatively normal lives.

How do I get porphyria?
The genes people inherit play an important role in causing porphyria. Genes are responsible for managing the production of proteins that control the cells in your body. In porphyria, the gene that provides the instructions for making the enzymes needed to produce haem has an abnormality, known as a ‘mutation’. This mutation reduces the amount of haem your body can produce.

People inherit two copies of genes, one from each parent. In most types of porphyria, people need to inherit only one copy of a mutated gene, this is called ‘autosomal dominant’ porphyria. In rarer porphyrias, including ADP and CEP, people need to inherit two copies of a mutated gene for the disease.

Genes are only part of the cause of porphyria, however. Most people who carry the genes that can cause porphyria do not actually have the disease. These people are ‘carriers’ or people with ‘latent porphyria’ and could pass the gene onto their children.

There are environmental factors that have an influence on whether people who carry the genes will become ill with porphyria. These can include excess alcohol, excess iron, exposure to oestrogen or other chemicals, viral infections and hepatitis C. The interaction of genetic and environmental factors is not well understood, meaning that for most patients it is not possible to predict or prevent the development of the disease.

What are the symptoms of porphyria?
Acute porphyrias are characterised by attacks of pain and other signs of neurological distress. In cutaneous porphyrias, the build-up of porphyrins and porphyrin precursors interacts with ultraviolet light from sun exposure to cause your skin to become very sensitive to light.

Symptoms do not usually appear until well after puberty and are seen more in women than in men (and more likely to occur during menstruation). The majority of people who inherit the disorder do not have attacks. Where symptoms do occur, they are sudden and can last for days or weeks.
Attacks of acute porphyria may unfold or progress with the following symptoms:

- anxiety, restlessness and insomnia
- severe abdominal pain
- pain in your arms, legs or back
- vomiting and constipation
- high blood pressure (hypertension)
- muscle pain, tingling, numbness, weakness or paralysis
- confusion, hallucinations and seizures
- breathing difficulties (respiratory paralysis), possibly requiring ventilation
- reddish coloured urine.

Skin exposed to sunlight is likely to become very fragile, where even slight contact may cause injury to your skin. Areas most at risk are those more commonly exposed, such as your face, neck, hands and feet. In some cases this can lead to permanent skin damage.

A combination of porphyria cutaneous tarda and chronic liver damage may place a person at much higher risk of developing liver cancer, known as hepatocellular carcinoma (HCC).

**Diagnosis**

As porphyria is very uncommon it is often missed or wrongly diagnosed by doctors. Diagnosis is difficult because most symptoms are non-specific, such as abdominal pain, and can often be caused by many other conditions. Even for people with porphyria, it is possible that symptoms can be caused by other underlying problems.

The way in which porphyrins accumulate and the enzyme deficiency that causes this to happen is unique to each porphyria. The doctors treating you cannot make a diagnosis or even distinguish between the various forms based on physical symptoms alone. They will have to carry out appropriate biochemical investigations and
correctly interpret the results of these to identify which form of the disease you have.

Tests will examine the following:

- **urine test** – if you have a form of acute porphyria, a urine test may reveal elevated levels of porphobilinogen and aminolevulinic acids, as well as other porphyrins. It is likely that your urine sample will be sent to a specialised laboratory for this test.

- **blood test** – if you have a form of cutaneous porphyria, a blood test may show an elevation in the level of porphyrins in the clear, liquid part of your blood (plasma).

- **stool sample test** – analysis of a stool sample may reveal elevated levels of some porphyrins that may not be detected in urine samples. This test may help doctors to determine the specific type of porphyria affecting you.

Since most types of porphyria are inherited, investigations should also be carried out on children and blood relatives of affected people.

**Prevention**

As porphyria is an inherited disorder, there is little people can do to avoid acquiring the condition. People whose parents have porphyria may want to take advice on precautions they can take to reduce their risk of developing the condition. Although you may not be able to prevent porphyria, there are a number of treatments and things you can do to manage your condition and prevent attacks.

**Treatment**

There is no cure for porphyria. Treatment is aimed at getting rid of or managing your symptoms.

Only drugs known to be safe in porphyria can be prescribed for treatment, as many medications, including common sleeping pills and antibiotics can trigger acute attacks. This underlines the importance of making others aware that you have the condition, and the specific form.

Treatment of acute porphyrias may include:

- stopping medications known or suspected to have triggered your symptoms
- medication to control pain. If pain is severe, opiate-based drugs such as pethidine or morphine are safe to be given. A sedative, chlorpromazine (thorazine) may be used to relax you and help you sleep. Similarly, rapid heart beat and hypertension can be helped with propranolol to slow your heart rate. Anti-epileptic drugs may be given to control convulsion or seizures
- oral and intravenous glucose (sugar) to help you maintain a high energy intake
- haem arginate, a medication that is a form of haem, given to reduce the need for your body to produce its own. Combined with glucose, this lowers porphyrin levels by reducing the formation of aminolaevulinic acid. It is used mainly for severe attacks and is likely to be given to you intravenously over several days. Haem arginate has a rapid effect and an improvement may be expected within one week.
Treatment of cutaneous porphyrias is aimed at reducing the amount of porphyrins in your body to help eliminate your symptoms. This may include:

- phlebotomy, also called venesection, a procedure similar to that used for blood donation in which a quantity of blood (usually up to 500 millilitres) is drawn into a blood donation bag via a needle placed in a vein in your arm. It is carried out to reduce the amount of iron in your body. Phlebotomy is most commonly used for PCT.

- blood transfusion, the opposite treatment to phlebotomy. This is used for CEP in order to treat anaemia, in which you lack enough red blood cells.

- a low dose of chloroquine, a drug given in tablet form twice a week.

- beta carotene, given daily for EEP. Made from the orangey-yellow pigment that gives many fruits and vegetable their colour, beta carotene is converted by the body into vitamin A, to promote healthy skin and eyes and to increase your skin’s tolerance to sunlight. It may also colour your own skin a slight orangey shade.

- a bone marrow transplant may be required for people with CEP, where the abnormal gene involved may also affect the formation of bone marrow.

### Looking after yourself

Following diagnosis, most people with porphyria are able to lead relatively normal lives by following simple measures to prevent symptoms occurring. With careful management, some patients are able to experience long periods of time without symptoms or enter remission.

To prevent acute attacks, it is sensible to avoid:

- taking or accepting medication without first checking that it is safe for you. A list of drugs that are considered safe in the treatment of porphyrias can be obtained from the organisations listed on page 20 of this leaflet

- illegal psychoactive drugs such as cannabis, ecstasy, cocaine, amphetamines and barbiturates

- smoking and drinking alcohol

- fasting or following diets that leave you low on energy.

Extra monitoring should be made during pregnancy, when oestrogen levels are elevated.

Wearing some form of medical identification such as a medic alert disc will alert staff to your condition in the event of any emergency treatment.

People with cutaneous porphyrias should stay out of the sun as much as possible. Even exposure to bright light through the windows of a building or car should be avoided. When outside it is advisable to wear sun-protective clothing and heavy sun block containing zinc or titanium.

PCT, the most common skin porphyria, is linked with iron-overload and may cause serious liver damage if not regulated. You may be asked to avoid food rich in iron, vitamin C supplements and high dose oestrogen via contraception.

As is the case in anyone who has a liver condition, alcohol should be avoided.
Diet and exercise
There is no specific diet recommended for porphyria disorders other than eating healthily and making sure meals are taken regularly. This is more important for people who have acute porphyria as they are more sensitive to the effects of certain foods and beverages. This means keeping up a steady intake of calories by eating plenty of carbohydrates.

People who have acute porphyrias commonly suffer fatigue. This may be due to symptoms affecting muscles and joints (such as pain, numbness and weakness) and the sleep disturbance this may cause. In some cases the effects of medication used to control symptoms may contribute to bouts of tiredness.

It is important that your muscles do not get out of condition or reduce in size (atrophy). For this reason it is likely doctors will encourage you to follow a daily exercise routine or to take part in moderate physical activity a few days a week to keep your muscles in shape and to help you sleep better.

You can obtain more detailed advice about diet and exercise from the organisations listed under ‘Who else can help?’ on page 20.

Complementary and alternative medicines
Many complementary and alternative medicines are available that may ease the symptoms of liver disease. But certain medications used in non-liver related disease can damage the liver. At present, healthcare professionals are not clear on the role and place of some therapies in managing liver disease. More research needs to be done on the use of these therapies. You may wish to discuss the use of these therapies with your doctor.

Useful words

**Acute** – a short sharp illness that may be severe but from which most people will recover in a few weeks without lasting effects.

**Acute attacks of Porphyria** – almost always start with severe pain which is usually in the abdomen but may also be felt in the back or thighs. Nausea, vomiting and constipation are common. Some people may become very confused during an acute attack and later find it difficult to remember details of their illness. An acute attack usually lasts for no longer than one or two weeks, but may be life threatening because of severe neurological complications like motor paralysis. Most people who have one or a few attacks of acute porphyria make a full recovery. They are then able to lead a normal life except that they need to take a few simple precautions to reduce the risk of having another attack. Women are over 3 times more likely to have an acute attack due mainly to female hormones.

**Acute porphyrias** – the condition mostly affects the nervous system. The skin is occasionally affected. Symptoms may include muscle pain or paralysis, seizures, disorientation, hallucination, bloody urine, hypertension and gastrointestinal problems such as vomiting, abdominal pain and
constipation. Acute porphyrias generally occur during adulthood and are rare before puberty or after menopause.

**Autosomal** – relating to the non-sex (‘X’ and ‘Y’) chromosomes.

**Biochemistry** – the study of chemical substances, processes and changes that occur in living organisms.

**Carbohydrate** – a substance that provide energy or fuel for your body. ‘Simple’ carbohydrates are sugars, as found in fruit, honey and jam. ‘Complex’ carbohydrates are starches, as found in bread, rice and potatoes.

**Chronic** – an illness that lasts a long time (more than six months), possibly for the rest of a person’s life.

**Cutaneous porphyrias** – the condition affects the skin but not the nervous system. The skin is highly sensitive to sunlight and exposure tends to trigger symptoms within minutes. Symptoms may include red, itchy, blistered, painful and swollen skin and bloody urine. The condition may develop during childhood.

**Expression** – the process where information encoded in a gene is converted into the structures and functions of a cell.

**Enzyme** – a protein that speeds up a chemical reaction within a cell, without being changed or used up in the reaction.

**Erythropoietic** – relating to the formation of red blood cells (erythrocytes) in the body.

**Gene** – a segment of a chromosome (or unit of DNA) that carries the instructions or code for making a specific protein or set of proteins responsible for, or contributing to, a specific physical trait or action.

**Hepatic** – anything relating to the liver.

**Inferior vena cava** – the large vein that carries blood back to the heart from the lower part of the body.

**Inflammation** – the first response of the immune system to infection, commonly characterised by heat, swelling, pain and tenderness.

**Metabolic** – relating to the break down and processing of substances in your body for growth and vitality.

**Mutation** – an occurrence where a gene undergoes a change or variation in the base sequence of its DNA. Some mutations result in the gene no longer coding for the correct protein, or producing a reduced amount of the protein.

**Neurocutaneous porphyrias** – the condition affects both the skin and the nervous system. Sunlight exposure tends to rapidly trigger symptoms.

**Protein** – the active molecule in cells that determine the physical structure of the organs and tissue that make up your body. Proteins also control the biological and chemical reactions within your body.
Who else can help?

**British Porphyria Association (BPA)**
Tel: 01474 369 231  
Email: helpline@porphyria.org.uk  
Web: www.porphyria.org.uk  
Through meetings, advice, counselling, published information and its website, the BPA aims to reach out to as many people as possible – patients, health professionals and those involved in research – to improve understanding of this rare condition.

**European Porphyria Initiative (EPI)**
Email: info1@porphyria-europe.com  
Web: www.porphyria-europe.com  
The EPI aims to present an up-to-date approach to the understanding of porphyria, focusing in particular on the prevention and treatment of acute attacks, providing information and support to families affected by porphyria, and supporting and encouraging medical research.

**The Cardiff Porphyria Service**
Web: www.cardiff-porphyria.org  
The Cardiff Porphyria Service specialises in the diagnosis and treatment of the porphyrias in the UK. The Service website has a range of information resources of interest to both health professionals and patients.

www.drugs-porphyria.com  
An international drug database for porphyria that provides a list of medicines available in the UK. Including both generic and UK trade names, the website provides a full list of the drugs are safe or unsafe for people with porphyria.

Further information

The British Liver Trust publishes a large range of leaflets about the liver and liver problems written for the general public.

Leaflets that you may find particularly helpful include:
- *Diet and liver disease*
- *Liver disease tests explained*
- *Liver transplantation*
- *Life after liver transplant*

**Contact us for more information:**
Tel: 0800 652 7330  
Email: info@britishlivertrust.org.uk  
Web: www.britishlivertrust.org.uk

This leaflet is for information only. Professional, medical or other advice should be obtained before acting on anything contained in the leaflet as no responsibility can be accepted by the British Liver Trust as a result of action taken or not taken because of the contents.

Special thanks

Dr Adrian Bomford, Reader in Medicine and Honorary Consultant Physician, Institute of Liver Studies, King's College Hospital, London.
Can you make a difference?

Liver disease is increasing alarmingly and the need to do more is greater than ever before...

For the British Liver Trust to continue its support, information and research programme, we need your help. We raise funds from many sources and a large proportion is donated by voluntary contributions. If you would like to send a donation it will enable us to continue providing the services that people need.

If you can help, please fill in the form on the page opposite.

If you wish to help us further with our work by organising or participating in a fundraising event or becoming a “Friend of the British Liver Trust” please:

Call us on
0800 652 7330

Email us at
info@britishlivertrust.org.uk

Make a donation via our website at
www.britishlivertrust.org.uk

or write to
British Liver Trust
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Ringwood, BH24 1HY

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Your name and address will be added to our computer database ensuring you are sent the latest information. If you do not wish to receive further information, please tick here.

Fighting liver disease
This patient information leaflet was produced with support of a donation from The James Tudor Foundation.

**British Liver Trust**
2 Southampton Road
Ringwood, BH24 1HY
**Tel:** 0800 652 7330  **Fax:** 01425 481335
**Email:** info@britishlivertrust.org.uk
**Web:** www.britishlivertrust.org.uk