Porphyria Cutanea Tarda (PCT)

The information in this leaflet is to help you understand more about porphyria cutanea tarda (PCT). The information is based on best available evidence and the consensus of the cutaneous porphyria working group of EPNET, https://porphyria.eu.

CONTENTS

1. What is Porphyria Cutanea Tarda (PCT)?

Porphyria cutanea tarda (PCT) is the commonest type of porphyria, affecting about one in 5,000 to one in 70,000 of the population, depending on the country. In PCT, large amounts of porphyrins are produced by the liver, accumulate in the body and cause the skin to become sensitive to light.

2. What causes PCT?

PCT is caused by reduced activity of an enzyme called uroporphyrinogen decarboxylase (UROD) (an enzyme is a protein inside our cells that converts one chemical substance into another). This reduced activity leads to a build-up of porphyrins in the liver from which they overflow into the blood stream and thus reach the skin. Skin problems usually start during adult years; 'tarda' means 'late'. The cause of the reduced activity of UROD is not fully understood but it is believed to result from various factors (predisposing factors – see list below) which interact with UROD and increase the chances of an individual getting PCT.

3. Is PCT inherited?

Most patients have a form of PCT that is not inherited. This type of PCT is called **sporadic or Type 1 PCT**. In Europe, about one quarter of patients have an inherited risk factor for PCT - and have **familial or type II PCT**. This is caused by inheritance of a mutation which inactivates one copy of the UROD gene, leaving the other to function normally. Everyone has two genes for UROD in each cell in their body; one inherited from their mother and one from their father. Inactivation of one of the copies results in a reduction in UROD activity in every cell to about 50% of normal. However, most family members who inherit the gene mutation will not develop PCT because other causes (predisposing factors) need to be present as well, reducing the level of activity in the liver cells to about 20% of normal.

4. What are the most important predisposing factors?

The following are the most important predisposing factors that have been identified. Most patients will have at least one.

- **Iron accumulation in the liver.** Almost all PCT patients have an increase in iron in the liver, which is believed to be the most important factor involved in the inactivation of the UROD enzyme. Some of these patients may also have inherited a condition called haemochromatosis that is responsible for too much iron accumulating in the body.
- **Regular alcohol consumption.**
- **Viral infections of the liver.** Hepatitis C is an important predisposing factor for PCT in many European countries.
- **Cigarette smoking**
- **Exposure to some industrial chemicals**
- **Oestrogen therapy.** For example as oral contraception or hormone replacement therapy (HRT).
- **Dialysis for kidney failure**

5. What are the symptoms of PCT?

Only areas of the skin exposed to sunlight are affected. These are most commonly the backs of the hands, the face and scalp and any other areas of skin regularly exposed. Porphyrins circulating through dermal vessels are activated when exposed to light, and emit free radicals that damage the junction between the outermost layer of the skin (the epidermis) and the underlying layer (the dermis) leading to a fragile skin. The consequences are that in sun-exposed areas even mild injury or everyday tasks may cause the skin to break or form large

fluid filled blisters that burst and heal slowly leaving scars and tiny white raised spots called milia. There may be changes in skin pigmentation, which can be increased or decreased, and an increased growth of fine hair on the cheeks and forehead. In addition to the skin problems, the urine may take on a dark colour due to excess of uroporphyrins excretion. Acute crises (the abdominal pain and nerve damage, often provoked by drugs or hormones), that occur in a group of porphyrias called the acute porphyrias DO NOT occur in PCT.

6. How is PCT diagnosed?

PCT is diagnosed by measuring porphyrins in samples of blood, urine and faeces. These tests look for the particular pattern of porphyrins associated with PCT. This is very important because other porphyrias can cause similar skin problems.

Your doctor should also test for the predisposing factors described above which are associated with PCT.

These will include blood tests for:

- liver function
- viral hepatitis, Human Immunodeficiency Virus (HIV)
- Iron status and haemochromatosis

As PCT is often associated with some evidence of liver damage – due to alcohol, excess iron, hepatitis C virus or the porphyria itself - your doctor may order an ultrasound examination of your liver to exclude scarring, too much fat in the liver or the presence of a liver tumour. Depending on the results of these tests, you may be advised to see another doctor, for example a liver specialist or haematologist.

The porphyrin pattern in PCT is so characteristic that other tests to identify the type of porphyria are not normally required. Members of families in which there is more than one patient with PCT should be offered genetic counselling and may require screening for Type II PCT. If a genetic cause for iron overload is found, close relatives should be seen to determine whether they should be followed up or treated for iron overload.

7. Can PCT be cured?

Although the underlying causes of PCT may not be curable, the condition can be well controlled and the porphyrin levels reduced to normal. It is important that known predisposing factors are controlled or treated as well. With appropriate treatment, the skin problems resolve slowly and eventually disappear though they may leave some scars. Relapse 2 or more years after successful treatment may occur. This is why patients with PCT, whatever the contributing or predisposing factors are, should continue seeing their doctor regularly. Recently, a cure for the hepatitis C virus infection has become possible with direct acting antiviral drugs (DAA), which cures the virus infection and the associated PCT.

8. How can PCT be treated?

The aim of treatment is to remove or decrease any predisposing factors, to reverse the inactivation of UROD enzyme and to remove the excess porphyrin that has accumulated in the body.
You are likely to be offered one of two specific treatments:

- Regular removal (usually every two weeks) of a unit of blood (the same amount as given by blood donors) to decrease iron levels. The medical term for this treatment is venesection. The body uses iron to make more blood and the process is repeated until enough iron has been removed – often 5 to 6 units of blood. This will take several months in most cases. If you also have haemochromatosis, venesection may be needed on a long-term basis. The lowering of liver iron concentrations results in improved function of UROD enzyme.

- Low-dose chloroquine or hydroxychloroqine (usually twice weekly tablet). It is important that only this very small dose is used, as larger doses can cause an acute illness. The chloroquine and hydroxychloroquine make the porphyrins more soluble and increase their excretion in the urine, which may result in some darkening of the urine. As only low doses of chloroqine or hydroxychloroquine are used, regular eye review is not generally required.

Both treatments are effective in most patients. The choice will depend on various factors, including which are considered to be the most important predisposing conditions in each patient. Occasionally both treatments may be required. In patients who cannot tolerate either of these two treatments, other options such as drugs that help remove iron from the body are available, although these are more complicated to administer.

Other measures:

- **Alcohol.** All alcoholic drinks should be avoided.
- **Cigarette smoking** should be stopped.
- **Oestrogen therapy.** Women on oestrogen treatments will be asked to stop taking them while the PCT is being treated. However once the PCT has been treated it may be possible to restart hormone treatment.
- **Iron supplements** should not be taken, unless you have clear evidence of iron deficiency.
- **Treatment for hepatitis C.** PCT in patients with hepatitis C may resolve with treatment with direct acting antiviral (DAA) drugs.

Occasionally skin symptoms may get worse and the urine can darken when treatment is started.

9. What can I do?

• **While treatment takes effect:** Avoid sunlight and protect your skin from light exposure. The skin will remain fragile and sensitive to bright sunlight for several months until treatment becomes fully effective. The skin damage in PCT is caused by the visible part of the sun's light spectrum, which means that ordinary sunscreens (which protect against ultraviolet light) do not work. Reflectant sunscreens based on titanium dioxide or zinc oxide cover will be more effective. Using a tanning cream containing dihydroxyacetone may block the light to some extent. You should avoid damaging the skin, by wearing protective clothing such as gloves (white cotton preferably), a hat (ideally brimmed or Foreign Legion-style), shoes rather than sandals, and minimising your exposure to the sun during this time. Wounds or broken blisters should be kept clean, and any skin infection treated promptly.

• **Reactions to other medications:** Unlike other types of porphyria, PCT does not cause acute porphyria crises due to other medications. Unfortunately some doctors and pharmacists confuse PCT with the "acute porphyrias" and may tell you to avoid certain medicines. In general, you can take whatever medicines your health requires.

10. Where can I get more information about PCT?

As PCT is uncommon, most general practitioners will have little experience of the condition. However, dermatologists see most people with PCT and may sometimes ask for advice from a porphyria specialist centre.

If you are concerned about the likelihood of passing the condition onto your children (familial PCT), you may be referred to a geneticist or porphyria specialist center for information. The content on the EPNET website is based on a consensus agreed by EPNET partners. Although there are a number of other sources of information, the majority of which are on the internet, they may not have been validated by porphyria specialists. Most give details about all the forms of porphyria.

Patient associations can be a good point of contact for information, networking and support. Porphyria patient groups in different European countries are listed on the European Porphyria Network website, https://porphyria.eu/content/patient-organizations and the Global Porphyria Advocacy Coalition (GPAC) website, https://www.gpac-porphyria.org.

Revised : February 2021