



## **ERYTHROPOIETIC PROTOPORPHYRIA and X-LINKED DOMINANT PROTOPORPHYRIA**

### **What are the aims of this leaflet?**

This leaflet has been written to help you understand more about erythropoietic protoporphyria (EPP), and a variant of EPP called X-Linked Dominant Protoporphyria (XLDPP). It explains what it is, what causes it, what can be done about it and where more information can be found about it.

### **What are erythropoietic protoporphyrias?**

The word 'erythropoietic' is associated with red blood cells ('erythro-') and their formation ('-poietic'). The porphyrias are a group of uncommon disorders caused by something going wrong with the production of chemicals known as porphyrins. These chemicals are the building blocks of haem, which, when combined with a protein (globin), forms haemoglobin, the material in red blood cells that carries oxygen round the body. In the case of EPP and XLDPP, there is a build-up of one of these porphyrins (protoporphyrin IX) in the blood, especially in the red blood cells. This leads to a sensitivity to sunlight.

### **What causes EPP and XLDPP?**

An enzyme is a protein that helps to convert one chemical substance into another. In EPP, there is a shortage of one particular enzyme, ferrochelatase, which normally helps to convert protoporphyrin into haem by adding iron to it. As a result of this enzyme deficiency, protoporphyrin levels build up in the blood. In XLDPP, a problem in the ALA-synthase gene causes an increase in activity of this enzyme which causes the protoporphyrin to build up in the blood.

As blood passes through the superficial blood vessels under the skin, the protoporphyrin absorbs the energy from sunlight and this sets off a chemical

reaction that can slightly damage surrounding tissues. The nerve endings in the skin interpret this as itching or burning pain, and if the blood vessels are affected, they can leak fluid, causing swelling.

The light that protoporphyrin absorbs is different from that which causes sunburn. Sunburn is caused by the shorter wavelengths of ultraviolet light (UVB), but in EPP the skin is more sensitive to longer ultraviolet wavelengths (UVA) and to visible light.

### **Are EPP and XLDPP hereditary?**

Yes, but there is not always a family history of the condition. Everyone has two copies of the ferrochelatase gene in each cell in their body (one coming from their mother and one from their father). In most families, EPP occurs when an affected individual inherits a gene for a severely underactive ferrochelatase enzyme from one parent, and a less severely affected gene from the other parent. The less severely affected gene is quite common, being present in around 10% of the general population, but it never causes EPP by itself. The overall chance of a patient affected by EPP having an affected child is low. The chance of a patient affected by XLDPP having an affected child is high. On average, 50% of the children of a patient affected by XLDPP will also have XLDPP. This is the main difference between EPP and XLDPP for patients. In other ways, the two conditions cause exactly the same problems for patients.

### **What are the symptoms of EPP and XLDPP?**

The symptoms of EPP and XLDPP are identical and typically start with abnormal sensitivity to sunlight. Skin exposure to sunlight causes tingling or itching within a few minutes, severe pain and burning then occur, which may be associated with redness and swelling. These symptoms can take several days to resolve.

During this time, the skin may feel extremely sensitive to temperature, light and touch. The light producing these changes need not be direct – light reflected off water and sand, or passing through window glass, including car windscreens, can also cause the symptoms.

EPP usually starts in childhood and affects males and females equally. XLDPP also starts in early childhood. Infants may cry or scream after being taken out into the sunlight; and older children may complain of severe pain and burning. A very small number of people who have been affected by EPP or XLDPP for many years may develop liver damage. Fortunately, this is rare.

## **What does EPP and XLDPP look like?**

Despite severe pain, there may be nothing abnormal to see on the skin. Sometimes there can be swelling of the skin, initially like a nettle rash. With time, some people develop thickening of the skin over their knuckles, and small scars on sun-exposed skin such as that on the cheeks, nose, and backs of the hands. However, these skin changes show wide variations between different individuals.

## **How are EPP and XLDPP diagnosed?**

The diagnosis is usually suspected from the history of the patient's symptoms and can be confirmed by a blood test. This measures the amount of protoporphyrin in the blood (plasma protoporphyrin) and in the red blood cells (erythrocyte free protoporphyrin). This test will also usually allow XLDPP and EPP to be distinguished. Some doctors will also ask for a stool sample to measure the level of protoporphyrin in the faeces. No urine tests are relevant to this condition except to exclude other types of porphyria.

Although it is unlikely that you will develop liver problems as a complication of EPP and XLDPP (this happens in less than 5% of patients), your doctor may monitor the way your liver is working by yearly blood tests. If there is any evidence of deterioration in liver function, there are certain interventions that may help to halt or reverse this. You may also be referred to a liver specialist. There is also an increased risk of developing gallstones in EPP and XLDPP.

As EPP and XLDPP affect the production of haemoglobin, it is not uncommon for people affected by EPP to be slightly anaemic. Your doctor will probably also measure your blood count to make sure that you are not becoming too anaemic.

## **Can EPP or XLDPP be cured?**

At present there is no cure for EPP or XLDPP.

## **How can EPP and XLDPP be managed?**

The aim of most treatments is to give your skin extra protection from sunlight, so that you tolerate sunlight better.

## **Self-care (What can I do?)**

It is sensible to avoid unnecessary exposure to sunlight. Other helpful measures include the wearing of protective clothing and the use of sunscreens:

- **Clothing.** Simple measures include the wearing of clothes made from tightly woven cloth, long sleeves, a hat (ideally brimmed or Foreign Legion-style), shoes rather than sandals, and gloves, particularly for driving.
- **Sunscreens.** As EPP is characterised by sensitivity mainly to visible light, conventional sunscreens that are formulated to protect against ultraviolet (particularly UVB) are usually not effective. Reflectant sunscreens that contain titanium dioxide or zinc oxide will be more effective as they cover UVA, UVB, and reflect visible light to a degree. In the UK there is a physical sunscreen made in Dundee ('physical' means the cream stays on top of the skin to deflect and scatter damaging UV rays away from the skin.) These are available in 3 colours (beige/coffee/coral pink.) This sunscreen can be obtained on prescription from Tayside Pharmaceuticals (see below for details). You can mix the different coloured creams together to match your own skin colour before applying or as you apply to the skin.
- **Analgesia.** Unfortunately, the pain is unresponsive to standard painkiller medications. Cold compresses and cool fanned air may be helpful.
- **Reactions to other medications.** EPP does **NOT** cause porphyria 'attacks' as a complication of taking certain medicines and anaesthetics, unlike some of the other types of porphyria. Some doctors and pharmacists confuse EPP with these other porphyrias and may tell you to avoid certain medicines. In general, you can take whatever medicines your health requires (the only medication to be cautious about, in the way described below, is iron).
- **Surgical operations.** In general, surgical operations are not a special concern in EPP. The exception is for EPP patients who have severe liver disease: burn injuries to skin and internal organs can happen from the strong lights found in operating theatres. If in doubt, seek advice from a specialist porphyria service.
- **Laser treatments for hair removal or eye surgery** have not been a problem in protoporphyria. However, before hair removal treatment, the doctor may irradiate a small area of the skin to be treated for the length of time it will take to do the hair removal to ascertain if the patient would react.
- **Iron supplementation.** You should not take iron tablets in EPP or XLDPP without involving your porphyria specialist. Iron sometimes

makes EPP better, but sometimes it can make it worse, and occasionally iron tablets/supplements trigger liver problems in EPP and XLDP.

The iron issue in EPP/XLDP is difficult for family doctors to diagnose because the blood results in people with EPP/XLDP often look similar to those from people who are not affected by EPP/XLDP but who have iron deficiency causing anaemia. However, this does not mean that the EPP/XLDP patient has iron deficiency.

The situation with iron is complicated. Patients with EPP/XLDP, like anyone else, can develop iron deficiency anaemia. But they can be prescribed iron sometimes when they do not need it, and iron occasionally can cause health problems in EPP/XLDP. It is therefore best to ask for advice from your Porphyria Specialist if your family doctor (or another doctor) tells you that you need to take iron tablets.

## **B. Medical treatments for EPP and XLDP include the use of:**

- **Beta-carotene.** This is derived from the chemical that makes carrots orange. Some people with EPP do find that taking beta-carotene capsules is helpful, but overall, there is no proof that they are an effective treatment. This medicine is considered to be safe, but may occasionally cause a slight tummy upset. Large studies showed there may also be an increased risk of lung cancer in smokers. Beta-carotene is available on prescription, the dosage required may be up to 200mg per day, is taken by mouth and usually gives the skin a slightly orange colour. In the UK, the only licensed preparation is a 3mg capsule. Higher strength preparations are available via a company called Clinigen (15 mg capsule). As these preparations do not have a product licence in the UK, they are imported from abroad and the companies require written confirmation from your consultant of the reason why these higher strength capsules are required. This is to satisfy the Medicines Control Agency that there is a need to import the product even though a licensed product is available in the UK.
- **Phototherapy.** Narrow-band UVB and PUVA therapy are types of ultraviolet light treatment used in dermatology departments. They involve careful exposure to artificial ultraviolet light, usually three times a week for about five weeks in the spring. Induced light tolerance is thought to work by causing a physical change i.e. allowing the skin to thicken slightly and develop a tan. This acts as a natural sun block and may improve tolerance to sun exposure over the summer. This treatment is helpful to some patients.

- **Alpha-MSH analogue medications:** These are promising new treatments. The only one which, to date, is licensed (though not funded and not available in the NHS) as a treatment for EPP is Afamelanotide (SCENESSE®). Results of clinical trials have shown that it is effective at reducing the photosensitivity in EPP. It involves an injection of an implant approximately the size of a very long grain of rice, that sits under the skin and self-dissolves within 2 months. It is not funded in the UK by the NHS, and this is the case in other countries because of the high cost. Other medications that are similar are currently being tested in clinical trials to see whether they are effective and there is cautious optimism that a medication of this type will be available to help patients with EPP in the future.

### **Osteoporosis in EPP**

Patients with EPP are at risk of thinning of the bones ('osteoporosis') developing, not just in older patients but sometimes in patients as young as those in their thirties. This is important because it can lead to some bones breaking fairly easily,

There are two reasons for this. One is a lack of weight bearing exercise because of the difficulty going outside. The second is that most patients with EPP have a low level of vitamin D, because sunshine causes vitamin D to form in the skin. You should make sure that you do enough weight bearing exercise, even in the spring and summer (either outside when it is dark or inside on an exercise machine). The exercise should be weight-bearing i.e. involves walking or running.

You should have your vitamin D level in your blood checked at least once a year. Most patients need vitamin D3 supplements in the long term to keep the vitamin D level high enough. The usual dose that is needed is 1000 Units/day of vitamin D3. Vitamin D3 supplements are widely available from health food shops and chemists.

### **Where can I get more information about EPP?**

As EPP is so uncommon, many general practitioners will have had little experience of dealing with it. Most people affected by EPP will be seen by a dermatologist, but if they too have little personal experience of the problem, then they may refer you to a colleague with expertise for investigations and discussion. If you are concerned about the likelihood of passing the condition onto your children, you may be referred to a geneticist for information about this. There are a number of other sources of information, most of which are on

the Internet. Most give details about all forms of porphyria, although a few specialise just in EPP.

**Links to patient support groups with detailed information:**

British Porphyria Association  
136 Devonshire Road  
Durham City  
DH1 2BL  
Tel: 0300 30 200 30  
Web: [www.porphyrria.org.uk](http://www.porphyrria.org.uk)

CLIMB – children living with inherited metabolic diseases  
176 Nantwich Road  
Crewe, CW2 6BG  
Tel: 0870 7700 326  
Web: [www.climb.org.uk](http://www.climb.org.uk)

Rare Connect: Connecting Rare Disease Patients Globally  
Porphyria Community  
Web: <https://www.rareconnect.org/en/community/porphyria>

American Porphyria Foundation  
Web: [www.porphyrriafoundation.org/](http://www.porphyrriafoundation.org/)

**Web links to detailed information:**

European Porphyria Network (EPNET)  
Web: [www.porphyrria.eu/](http://www.porphyrria.eu/)

Porphyria South Africa  
Web: <http://www.porphyrria.uct.ac.za/>

**Other useful information:**

Tayside Pharmaceuticals  
Ninewells Hospital  
Dundee, DD1 9SY  
Tel: 01382 632052

**This leaflet aims to provide accurate information about the subject and is a consensus of the views held by representatives of the British**

**Association of Dermatologists: individual patient circumstances may differ, which might alter both the advice and course of therapy given to you by your doctor.**

*This leaflet has been assessed for readability by the British Association of Dermatologists' Patient Information Lay Review Panel*

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