



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 tells you what it is, what causes it, what can be done about it and where you can find out more about it.

What are erythropoietic protoporphyrias?

The word 'erythropoietic' means associated with red blood cells ('erythro-') and their formation ('-poietic'). The porphyrias are a group of uncommon diseases 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) in the blood, especially in the red blood cells. This leads to asensitivity 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, which has only recently been discovered, a mistake in the ALA-synthase gene causes an increase in activity of this enzyme and produces too much protoporphyrin which builds up in the blood.

As blood passes through 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 ordinary sunburn. Usually 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 genes for ferrochelatase 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 about 10% of the general population, but it never causes EPP by itself. The genetics is quite complex and advice from your local genetics service may be useful.

In XLDPP, the faulty gene is carried on the X-chromosome. Males are usually therefore more severely affected (they only have one X chromosome) and cannot pass on the condition to their sons (they only pass on their Y-chromosome). Females have two copies of the gene, one of which is suppressed in their cells. This is a random event and the proportion of normal and faulty enzymes can vary widely, as do their symptoms.

What are the symptoms of EPP and XLDPP?

The symptoms of EPP and XLDPP are identical and typically start with abnormal sensitivity to sunlight. Exposure to sunlight causes tingling, itching or burning, which may be associated with redness and swelling. These symptoms usually occur within a few minutes of skin exposure to sunlight, and often take hours or days to resolve. During this time, the skin may feel more sensitive than usual to extremes of temperature. 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, but as explained above females can have a milder form of the condition. Infants may cry or scream after being taken out into the sunlight; and older children may complain of burning and try to wave their hands in the air, or put them into cold water to try to relieve the pain. A very small number of people who have had EPP or XLDPP for many years may develop liver damage. Fortunately this is rare.

What does EPP and XLDPP look like?

Despite severe discomfort, 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 variation between different individuals.

How are EPP and XLDPP diagnosed?

The diagnosis is usually suspected from the story, 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 will also be referred to a liver specialist.

As EPP and XLDPP affect the production of haemoglobin, it is not uncommon for people with 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.

A. 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 are based on titanium dioxide or zinc oxide will be more effective as they cover UVA, UVB, and visible light to a degree. In the UK there is a physical sunscreen made in Dundee, available in 3 colours (beige/coffee/coral pink). This sunscreen is available 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.
- **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.
- **Surgical operations.** During surgery, EPP individuals may be at risk of burn injuries to skin and internal organs exposed to the strong lights found in operating theatres. This is particularly the case in those with liver failure. 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.

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 find that taking beta-carotene capsules is helpful. The capsules are available on prescription (supplier details are given at the end of the sheet), are taken by mouth, and usually give the skin a slightly orange colour. 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, and the dosage required may be up to 200mg per day. In the UK, the only licensed preparation is a 3mg capsule. Higher strength preparations are available via a company called IDIS (30 mg capsule), or 25 mg capsule from Durbin PLC. 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. The contact details for IDIS can be found at: <http://idispharma.com/> and Durbin PLC at: www.durbin.co.uk.
- **Antihistamines.** These tablets or syrups may help the few people for whom the nettle rash response of the skin is a major problem.
- **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. Although home phototherapy is not widely available in the UK yet, this is likely to change in the near future.
- **MSH (afamelanotide).** Afamelanotide (SCENESSE®) acts by increasing the levels of melanin (pigment) in the skin, which shields the skin against sunlight. Afamelanotide is currently under investigation, but is not yet a licensed treatment in the UK. Afamelanotide is delivered via a subcutaneous dissolving implant (sits under the skin) approximately the size of a very long grain of rice. Results to date suggest that the drug is well tolerated.

Vitamin D advice

The evidence relating to the health effects of serum Vitamin D levels, sunlight exposure and Vitamin D intake remains inconclusive. Avoiding all sunlight exposure if you suffer from light sensitivity, or to reduce the risk of melanoma and other skin cancers, may be associated with Vitamin D deficiency.

Individuals avoiding all sun exposure should consider having their serum Vitamin D measured. If levels are reduced or deficient they may wish to consider taking supplementary vitamin D3, 10-25 micrograms per day, and increasing their intake of foods high in Vitamin D such as oily fish, eggs, meat, fortified margarines and cereals. Vitamin D3 supplements are widely available from health food shops.

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 with 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 complex area. 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:

British Porphyria Association
136 Devonshire Road
Durham City
DH1 2BL
Tel: 0300 30 200 30
Web: 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

Rare Connect: Connecting Rare Disease Patients Globally
Porphyria Community

Web: <https://www.rareconnect.org/en/community/porphyria>

American Porphyria Foundation

Web: www.porphyrifoundation.com

Web links to detailed information:

European Porphyria Network (EPNET)

Web: www.porphyr-europe.org

Porphyria South Africa

Web: <http://www.porphyr-uct.ac.za/>

Other useful information:

XP Support Group (for those with XP and other photosensitive conditions)

<http://www.xpsupportgroup.org.uk/>

Xeroderma Pigmentosum Society (for those with XP and other photosensitive conditions)

<http://xps.org/wordpress/>

Tayside Pharmaceuticals

Ninewells Hospital

Dundee, DD1 9SY

Tel: 01382 632264

For details of source materials used please contact the Clinical Standards Unit (clinicalstandards@bad.org.uk).

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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