CONGENITAL ERYTHROPOIETIC PORPHYRIA

What are the aims of this leaflet?

This leaflet has been written to help you understand more about congenital erythropoietic porphyria. It tells you what it is, what causes it, what treatment is available, how to manage the symptoms, and where you can find out more about the condition.

What is congenital erythropoietic porphyria?

Congenital erythropoietic porphyria (CEP), also called *Günther's disease* after the doctor who first described it, is the rarest of the porphyrias. It is estimated that about 1 in every 2-3 million people are affected by CEP, which affects males and females equally, and occurs in all skin types.

The word 'congenital' means a condition that exists at birth and often before birth, or that develops during the first month of life; 'erythropoietic' means associated with red blood cells and their formation.

The porphyrias are a group of inherited disorders in which there is abnormally increased production of substances in the body called *porphyrins*. Porphyrins are very important as they form haemoglobin that carries oxygen around the body in the red blood cells. The production of haemoglobin involves a chain of reactions in which one porphyrin is converted to another. If there is a block in the chain of reactions, there will be a build-up in the body of a specific porphyrin depending on where the block occurs. Porphyrins in high concentration are damaging to tissues. The problems caused by the different porphyrias relate to the particular porphyrin that accumulates. In the case of CEP, there is a build up of one of these porphyrins called *porphyrinogen* in the bone marrow, blood and urine and this leads to the symptoms and signs of CEP.

What causes CEP?

An enzyme is a protein that helps to convert one chemical substance into another. In CEP, there is a shortage of one particular enzyme (uroporphyrinogen III synthase), which normally helps to convert porphyrinogen into uroporphyrinogen III that is essential to form haemoglobin in red blood cells. As a result of this enzyme deficiency, porphyrinogen levels build up in the blood. As blood passes through the skin, the porphyrinogen absorbs the energy from sunlight and this sets off a chemical reaction that can damage surrounding tissues. The light that porphyrinogen absorbs is different from that which causes ordinary sunburn. Usually sunburn is caused by the shorter wavelengths of ultraviolet light (UVB), but in CEP the skin is more sensitive to visible light and to longer ultraviolet wavelengths (UVA).

Is congenital erythropoietic porphyria hereditary?

Yes. The parents of someone with CEP have no symptoms of the condition and are called *carriers*. Each of them has a mutation in one of their two CEP genes. There is a 1 in 4 risk that each child born to 2 carriers will inherit the abnormal gene from both parents and thus develop the condition. This form of inheritance is called *autosomal recessive*.

What are the symptoms of congenital erythropoietic porphyria?

Individuals with CEP may not have all of the problems described in this leaflet as the severity of the condition varies. Usually, the disease presents with symptoms or signs soon after birth or in early childhood, but sometimes onset of disease is delayed until the teenage years or early adulthood.

- Red urine is usually the first sign noticed in newborn babies with CEP. The intensity of the redness can vary from day to day.
- The teeth have a reddish discoloration.
- The skin is very sensitive to light, especially direct sunlight, it may cause blisters or ulcers, which heal to leave scars. This most commonly happens at sun-exposed sites, for example the backs of the hands, the face, ears and nose; the eyes may also be sensitive to bright sunlight or artificial light that can cause ulcers and scarring. With time, some patients lose their eyelashes, making their eyes easily irritated by small particles of dust and fibre.
- Increased fragility of sun-exposed skin can lead to scarring and disfigurement on affected skin such as the face (the ears, nose, mouth) and the hands.

- The skin may take longer to heal after injury or blistering, and become infected.
- Anaemia, which varies in severity, is common in CEP. Anaemia develops because porphyrin damages red blood cells leading to tiredness, shortness of breath following minimal exertion and skin pallor.
- The spleen, which normally removes damaged red blood cells, can gradually enlarge and cause worsening of the anaemia and a reduction in the number of platelets (the blood cells that help to form blood clots to stop bleeding) and white cells in the blood (the blood cells that fight infections). This can lead to an increased risk of bleeding (such as repeated nose bleeds) and infections.
- CEP can occasionally cause thinning of the bones (osteoporosis), which can lead to bone fractures following minor injury.

What does congenital erythropoietic porphyria look like?

- Repeated blisters and ulcers can cause extensive scarring in sun-exposed skin and permanent bald patches on the scalp.
- Some individuals may develop darkening of sun-exposed skin.
- Excess body hair may develop, especially on the face and backs of the hands.

How is CEP diagnosed?

CEP may be suspected in children (or rarely in adults) who present with the problems described in this leaflet. The diagnosis is confirmed by measuring porphyrin levels in the blood, urine and faeces. These samples need to be protected from light until tested. A blood sample may also be taken to look for changes in the genes.

Testing for CEP in pregnancy is not offered routinely. However, CEP *can* be diagnosed in pregnancy in families where there is already a child with CEP. In this situation, cells taken from the fluid surrounding the baby in the womb (amniocentesis) or from the placenta, at 3 to 4 months into the pregnancy, are checked for the gene mutations causing CEP.

Can CEP be cured?

Currently, the only available cure for CEP is a bone marrow transplant (BMT) This involves transplanting healthy bone marrow from another person (the

donor) to the person with CEP (the recipient). Following successful BMT, the symptoms of CEP such as photosensitivity and anaemia will improve. However, the scarring from previous damage to the skin is permanent.

For BMT to succeed, the bone marrow of the donor needs to be a good match with the recipient. BMT is a high-risk procedure, and is currently reserved for those severely-affected individuals who have a bone marrow donor that is a close match.

Bone marrow transplantation can be effective but long term results are unknown and the procedure can be complicated by life threatening infections.

Research is underway to cure CEP with gene therapy. This would involve correcting the abnormal gene in the affected person. It is hoped that this research will make good progress over the next decade.

How can CEP be treated?

The treatment of CEP is aimed at preventing scarring of the skin and eyes, and reducing the complications. Strict avoidance of sun exposure is vital for these patients. Some or all of the following measures may be needed:

- ***Clothing:*** Protection of exposed skin from direct sunlight is required to prevent blistering and scarring. This should include the routine use of gloves, a broad brimmed hat, scarf, long sleeves, high collars and long trousers.
- The eyes should be protected by tinted, wrap-around sunglasses.
- ***Sunscreens:*** As CEP 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, the SPF (sun protection factor) number tells you how effective the sunscreen is for UVB, and the star rating (usually found on the back of the bottle, with a maximum 4 stars) gives a measure of the UVA protection.
- A 'tinted' reflectant sunscreen is available on prescription from Dundee Pharmaceuticals in three colours: coral pink, beige, and coffee. These can be mixed to obtain a good colour match with your skin.
- ***Surgical Operations:*** During surgery, CEP individuals are 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. Measures to reduce risks of surgery include shielding all lights using a yellow-coloured acrylate filter to cut off light wavelengths below about 530nm (such as TA81 XSR (Madico) or Bexfilm U (Summerside Blinds)). Likewise, windows adjacent to patients in areas such as wards should have filters applied.

- Curtains or blinds in the house and workplace may be needed to reduce the intensity of visible light. Some people may need to apply special photo-protective window films to the windows of their car and home in order to block out UVA and UVB light. These protective films may stop working and need replacing after about five years. Some car manufacturers offer UV protective glass as standard or as an optional extra, however most car windows do not block UV light. Your dermatologist or a patient support group may be able to advise you about suppliers of UV protective film. The British Photodermatology Group has released a consensus statement on UV protective films.
- Skin camouflage may be used to conceal scarring.
- Skin on light-exposed areas should be protected from cuts and grazes to prevent long-term scarring. This can be helped by keeping the skin well-moisturised and by wearing gloves.
- Skin ulcers need to be kept clean, dressed appropriately and infection treated in order to help healing.
- Repeated scarring of the skin, especially of the fingers, can restrict movement of joints. Regular, gentle hand exercises may help to delay or prevent this. Occupational therapy may be needed for those who have developed restricted hand movement.
- Blood transfusions may be needed to treat anaemia. Occasionally, removal of the spleen is necessary.
- Thinning of bones (osteoporosis) may require treatment with oral medication.
- Good oral hygiene is important to prevent tooth decay. If opening the mouth is restricted due to scarring around the mouth, a soft children's toothbrush or an electric toothbrush may be easier to use and cause less damage to the gums.
- There are some reports of the benefits of oral medication in CEP for example, Beta-carotene may be use to protect the skin from the light, Hydroxyurea can be used in transfusion dependant patients and low dose chloroquine to increase excretion of porphyrins.

Can medications make CEP worse?

CEP is **not** made worse by any medications. Therefore, unless the person is allergic or intolerant to a medication, individuals with CEP have **no** restrictions in taking any form of medication.

What other precautions are required for CEP?

If an individual with CEP needs an operation, exposure to the very bright lights of an operating theatre may result in damage to the internal organs. Theatre staff should ensure that the amount of light is minimised.

Where can I get more information about CEP?

Web links to detailed leaflets:
http://dermnetnz.org/systemic/cep.html

Links to patient support groups:

British Porphyria Association (BPA)
Web: www.porphyria.org.uk

European Porphyria Initiative (EPI)
Web: www.porphyria-europe.org

Children living with inherited metabolic diseases (CLIMB)

Web: www.climb.org.uk/IMD/Charlie/CongenitalErythropoieticPorphyria.pdf

British Association of Skin Camouflage (NHS and private practice)
Tel: 01254 703 107
Email: info@skin-camouflage.net Web: www.skin-camouflage.net

Changing Faces
Tel: 0300 012 0276 (for the Skin Camouflage Service)
Email: skincam@changingfaces.org.uk Web: www.changingfaces.org.uk

Skin Camouflage Network (NHS and private practice)
Helpline: 0785 1073795
Email: enquiries@skincamouflagenetwork.org.uk
Web: www.skincamouflagenetwork.org.uk

Other useful information:

Tayside Pharmaceuticals

Ninewells Hospital
Dundee, DD1 9SY
Tel: 01382 632052

For details of source materials use 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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PATIENT INFORMATION LEAFLET
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