Information for patients

# ACUTE PORPHYRIA

**Information for people with acute intermittent porphyria, variegate porphyria or hereditary coproporphyria and their families.**

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## ACUTE PORPHYRIA

### 1. WHAT IS ACUTE PORPHYRIA?

Acute porphyria is a term that includes three similar inherited diseases:acute intermittent porphyria (AIP), variegate porphyria (VP) and hereditary coproporphyria (HCP). They are grouped together because acute attacks of porphyria occur in each one. These attacks are uncommon and are often difficult to diagnose. In most European countries, about 1 in 75000 people suffer from them.
Acute intermittent porphyria is the commonest type. In this disease, only acute attacks occur and the skin is never affected. If you have variegate porphyria or hereditary coproporphyria, your skin may also be affected. In variegate porphyria, the skin changes and attacks of acute porphyria may not occur at the same time.

### 2. WHAT IS AN ACUTE ATTACK OF PORPHYRIA?

Acute attacks 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. Convulsions and muscular weakness, which may lead to paralysis, are less common symptoms. Pulse rate and blood pressure may increase but rarely to dangerous levels. 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. If paralysis occurs, recovery is gradual but slow.
Acute attacks are often provoked by drugs, alcohol, and hormonal changes, for example, those associated with the menstrual cycle. Infections and stressful situations may also precipitate an acute attack. The most common age for an acute attack is from the late teens to the forties. They are extremely rare in children before puberty. Most people have only one or a few acute attacks;only a minority suffer repeated attacks, sometimes over several years. Although acute attacks can be very severe, particularly if precipitated by drugs or alcohol, nowadays they are rarely fatal.
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.

## 3. HOW MANY TYPES OF PORPHYRIA ARE THERE?

Altogether there are seven main types of porphyria, including the three acute porphyrias mentioned above. Most of the others affect only the skin. They are called porphyrias because they cause accumulation of chemicals called porphyrins (purple-red pigments named from the Greek for purple) or the simpler chemicals, often called “precursors” (ALA and PBG) that are used up by the body to make porphyrins.

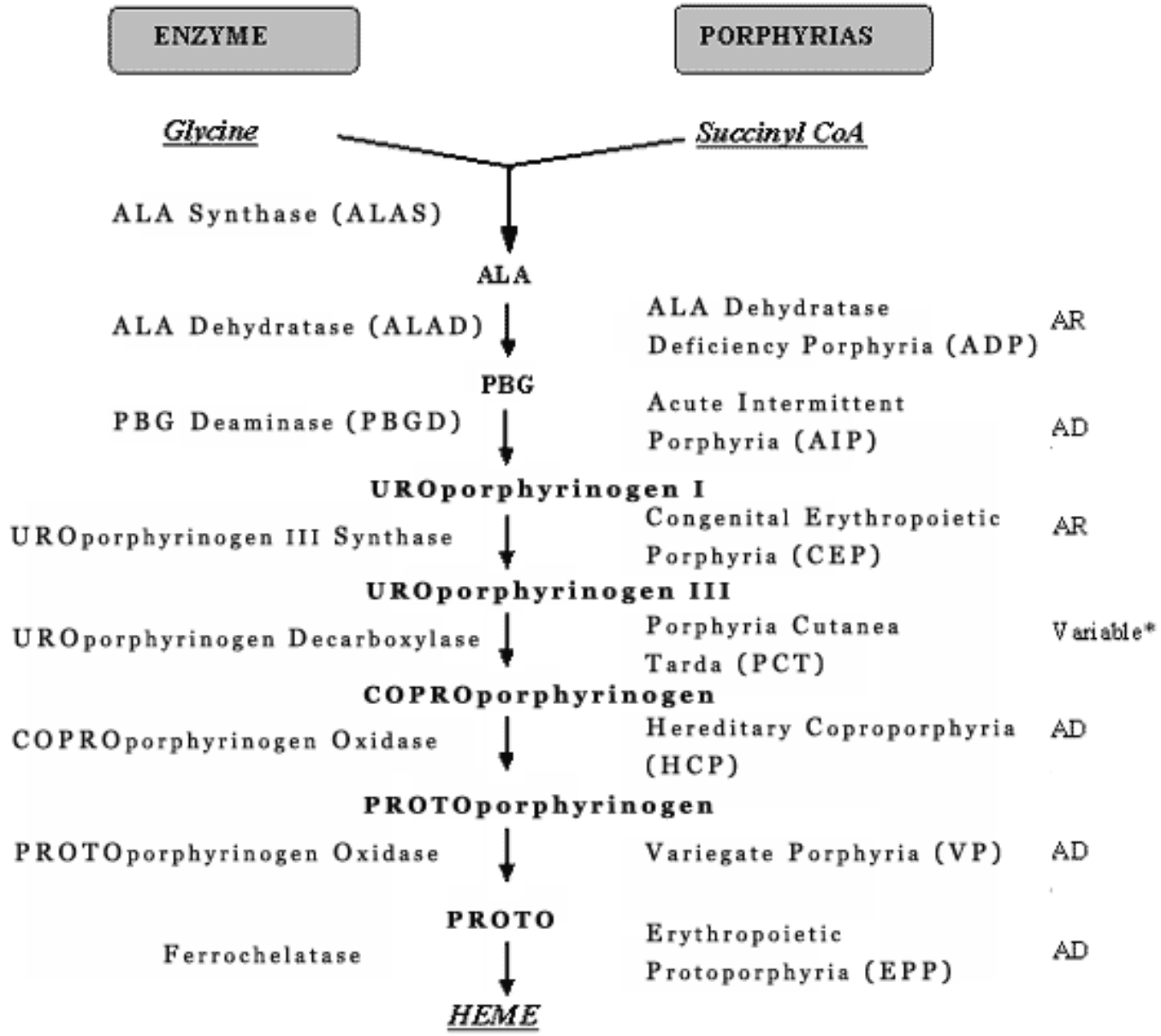


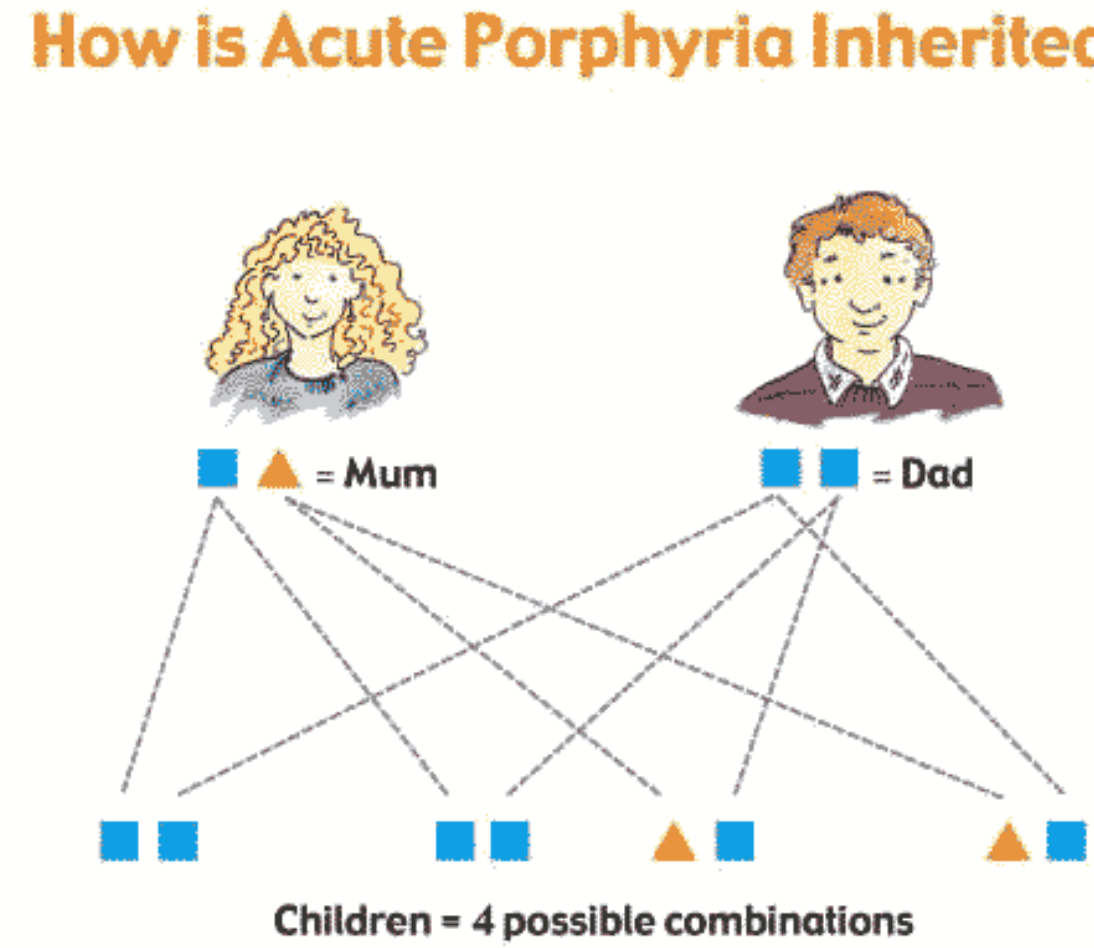

Fig.1: Classification of the major human porphyrias. ALA: delta-aminolevulinic acid; PBG = porphobilinogen; HEP = hepatoerythroporphyria. *Autosomal dominant inheritance has been documented in familial porphyria cutanea and recessive inheritance has been documented in HEP

Porphyrins are important in the body because they combine with iron to form heme, a red pigment which has the vital function of enabling the body's cells to use oxygen. All the porphyrias are due to a specific enzyme[1] defect along the heme biosynthetic pathway (see above diagram) The acute porphyrias are metabolic disorders that affect biochemical processes mainly in the liver. They do not cause blood disease or acute liver disease. When porphyrins accumulate in the skin, it becomes very sensitive to sunlight and this causes the skin symptoms of porphyria. Accumulation of the simpler chemicals in the liver leads to acute attacks of porphyria.
If you are suspected of having a porphyria, it is important for you to find out which type of porphyria you have because the inherited abnormality and symptoms are different in each one.

1. Enzyme : in our cells the enzymes are the "biological workers" that make all the biochemical processes possible

## 4. HOW IS ACUTE PORPHYRIA INHERITED?

The specific enzyme defect in each type of acute porphyria is the end result of an alteration in an hereditary particle of DNA known as a gene. Therefore a different gene is altered in each type of acute porphyria. This alteration is inherited so that each person with porphyria will often have a number of relatives who will also have inherited the altered gene. This means that when two or more people are affected in the same family they will all have the same disease. A person newly diagnosed with porphyria will often have a number of relatives, both close and distant, who will also have inherited the altered gene responsible for the type of acute porphyria in their family. Many of these relatives may not know that they have inherited an acute porphyria gene and that they are therefore at risk of developing an acute attack and in variegate porphyria and hereditary coproporphyria, skin disease.



of developing an acute attack

**This is an example of the inheritance of an acute porphyria. In this diagram mum is suffering from porphyria. She is carrying one normal gene and one altered (mutated) gene .**
**Of course, in another family dad could be suffering from porphyria.**
**In each case the probability for each child to inherit porphyria is one in two (50%).**

The gene alteration responsible for each type of acute porphyria is passed down through families in what is called an autosomal dominant pattern. Genes, which contain the blueprint for all the components required by the body, usually occur in pairs. One of each pair is inherited from each of our parents. Sometimes a small error can occur in the copying of one of these genes resulting in a permanent gene alteration which is called a mutation. When a mutation in only one of the pair of genes causes a disease, as it is the case in the acute porphyrias, it is called an autosomal dominant mutation. This altered gene (mutation) may then be inherited from parent to child and the risk of an affected person passing this gene on to any of his or her offspring is one chance in two (see above diagram). This risk is the same even if the affected person has never had any symptoms of porphyria. Thus the disease often appears to have “skipped a generation”. Of course, If you have not inherited the altered gene, you cannot pass it on to your children.

## 5. WHAT IS THE RISK OF SYMPTOMS AMONG THOSE WHO HAVE INHERITED AN ACUTE PORPHYRIA GENE?

Not all people who inherit a gene mutation for one of the acute porphyrias will develop an acute attack. It is estimated that at least three-quarters of people who inherit acute porphyria will never experience an acute attack of porphyria. In those who do become ill, it appears that additional factors are usually required for an attack to occur. Our knowledge of these factors is incomplete but among the most important are a number of drugs, some of which are widely used, and alcohol. However acute attacks do occasionally occur in the absence of any identifiable provoking factor. Experience over many years has shown that if people who have inherited one of the acute porphyrias are careful to avoid certain drugs, alcohol and other known factors that may provoke an acute attack, their chance of becoming ill is much reduced.

## 6. HOW IS AN ATTACK OF ACUTE PORPHYRIA DIAGNOSED?

For diagnosis of an attack of acute porphyria and identification of the type of porphyria, samples of urine, blood and stools (faeces) need to be carefully tested in a laboratory that has an expertise in porphyrias. The tests measure the concentration of porphyrins and their precursors ALA and PBG which will be very high in a patient with an attack of acute porphyria. It is important that these tests are carried out as soon as possible after the start of the illness as an accurate diagnosis may be difficult to establish after recovery from an acute attack, especially after several months or years.
In a patient who is known to have inherited an acute porphyria, it may be difficult to decide whether an illness is an attack of acute porphyria or caused by something else. In this situation, urine and, sometimes, other tests can often help your doctor to decide whether you are suffering from an acute attack or some other illness. It is important that people with porphyria should not attribute all their illnesses to porphyria. If they do, common but potentially serious conditions like appendicitis may be overlooked.

## 7. WHEN IS THE BEST TIME TO BE TESTED FOR AN ACUTE PORPHYRIA?

The best time to be tested for porphyria is at the earliest opportunity. In practice, this means that families should be offered screening for acute porphyria as soon as possible after a relative has been found to have the condition. When one or other parent is already known to have an acute porphyria, their children should be tested as soon as practicable. It is worth enquiring about this during pregnancy as your doctor will then be able to find out when your baby should be tested. In some cases, it is now possible to test baby at birth but it may be necessary to wait until your child is one year old or, occasionally, even older.
There are two main advantages of early diagnosis. First, those who are found to have inherited one of the acute porphyrias can be advised about how to reduce the risk of an acute attack. Second, if an

acute attack does develop, your doctor will be able to make the diagnosis and start special treatment early. The symptoms of an attack of acute porphyria are not always easy to recognise and, if the condition is not already diagnosed, there is a risk that your doctor will use drugs that may make the attack worse or may even think that an operation is necessary.

## 8. HOW ARE RELATIVES SCREENED FOR ACUTE PORPHYRIA?

For relatives who have not had an acute attack, and especially for children, urine testing is usually unhelpful. For these people, special tests on blood, and sometimes urine or faeces as well, need to be carried out in a specialist reference laboratory. For some families, it is now becoming possible to use DNA tests to detect the gene mutation that causes porphyria. DNA tests are more accurate than other methods but are complicated and are not yet available for all families. Your doctor should be able to arrange specialist testing for you. If you live a long way from a specialist porphyria laboratory, the samples can easily be sent by post following specific advice.

## 9. WHAT CAN I DO TO REDUCE THE RISK OF HAVING AN ACUTE ATTACK?

Many acute attacks are precipitated by controllable or avoidable factors such as drugs, alcohol, fasting (including dieting) or hormones.

### Drugs

People with acute intermittent porphyria must take great care with medication, as many chemical agents are capable of inducing an acute attack. **It is important ALWAYS to check the safety of any medicine or remedy with your doctor.** This includes prescription medicines as well as over-the-counter treatments, tonics and herbal remedies, some of which have been known to cause attacks. While over 100 drugs are considered suspect, there are many other drugs available and good alternatives can almost always be found.

Some people with porphyria may occasionally need a drug, perhaps for a serious illness, that carries some risk of provoking an acute attack or which has been introduced so recently that there is little information about its effect on porphyria. In this situation, your doctor, after fully discussing and evaluating the risks, if necessary, in consultation with a porphyria specialist, may decide to prescribe the drug for you with special follow-up.

Even though acute attacks are very rare before puberty, it is safest for children if they also avoid all drugs that are not known to be safe in porphyria.

The response of people with porphyria to drugs that have been reported to produce acute attacks in others is unpredictable in that a reaction does not invariably follow in every case. When there is a reaction, it always takes the form of an acute attack, which develops within days of taking the provoking drug. **Reactions such as dizziness, feeling faint, allergies or short-lived skin rashes, which may occur immediately or very soon after taking the drug are common after taking drugs and rarely have anything to do with porphyria.**

### Alcohol

While many doctors experienced in the care of those with acute porphyria strongly recommend absolute avoidance of alcohol, some people may find this recommendation difficult to follow. Experience has shown that people who have experienced an acute attack greatly reduce the risk of further attacks if they become teetotal for life. For those shown by testing to have inherited the gene responsible for one of the acute porphyrias but who have not experienced an acute attack, it is best that they avoid alcohol. However, if this proves impossible a reasonable compromise is to keep intake as low as practicable and, in particular, to avoid heavy red wines, brandy and other liqueurs.

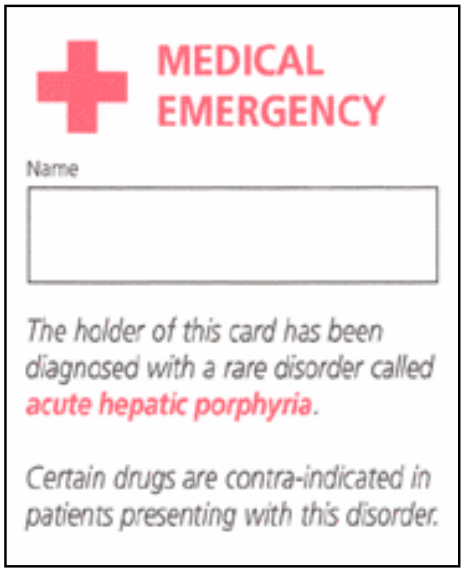
### Diet

Low calorie diets, such as those used to reduce weight, and prolonged periods with little food may provoke an acute attack. It is therefore important to keep to a normal diet with regular meals, eating enough to maintain a desirable body weight. People who have had an acute attack should obtain advice from a dietician about how this is best achieved for their particular circumstances. At least three regular meals should be taken each day;some people, particularly women with pre-menstrual

problems, may find it easier to eat small meals every three hours rather than three normal sized meals.

Patients with severe porphyria, particularly those who have repeated attacks, may need special dietary advice from their doctor and a dietician. If you are overweight, are found to have an acute porphyria and wish to lose weight, you should consult your doctor about the sort of diet that will allow you to lose weight gradually but safely.

### Medical alert card / Warning jewellery




It is important to wear a wrist bracelet, neck pendant and/or carry a card, that warns that you have porphyria, at all times. Such warning is particularly helpful in emergencies when you may not have an opportunity to explain that you have porphyria.
Porphyria warning cards may be obtained by contacting a specialist porphyria centre in your country *(more about porphyria specialist centres)*.
Details on warning jewellery can be obtained from the MedicAlert Foundation,www.medicalert.co.uk.
MedicAlert Foundation International currently serves members in over 50 countries.

## 10. SPECIAL PROBLEMS

### Anaesthetics and surgical operations

You must tell your surgeon and anaesthetist in advance that you have porphyria. A special anaesthetic that is safe in porphyria will be needed.

### The dentist

You should tell your dentist that you have an acute porphyria. Dentists often use local anaesthetic agents and the safety of at least one of these has been questioned in the past.

### Immunisations

All vaccines licensed for human uses are safe to administer to people who have an acute porphyria.

## 11. PARTICULAR ISSUES FOR WOMEN

Women are at least three times more likely than men to experience an acute attack, due mostly to female hormones, particularly progesterone. This hormone is found in the combined oral contraceptive (the pill), as well as in hormone replacement therapy (HRT) which is frequently prescribed for post-menopausal women. Oral contraceptive and HRT preparations containing progesterone or related compounds (progestogens) should be avoided, if at all possible, by women with an acute porphyria. Injectable and implantable long-term hormone preparations are very dangerous and must always be avoided.
In special circumstances, where the risk is low and the benefits high, your doctor may consider, after discussion with you and, if necessary, after consultation with a porphyria specialist, that the use of progestogen-containing preparations, particularly in replacement doses given through the skin from patches, is justified.

### Pre-menstrual symptoms

In some women, attacks are clearly related to the pre-menstrual phase of the menstrual cycle and

your doctor may need to consider a number of treatment options such as using special hormones to suppress your periods for 1-2 years. If you do need this sort of treatment, it needs to be done under close supervision by a doctor and will need regular monitoring.

### Pregnancy

Though nearly all pregnancies are uneventful, there is a small increased risk of having an acute attack during or after pregnancy. However, the chances and dangers of such an acute attack are much diminished if porphyria has been previously diagnosed. It is therefore very important for the doctors providing care during pregnancy to know that you have an acute porphyria.

## 12. TREATMENT OF ACUTE ATTACKS

### Importance of early recognition and accurate diagnosis:

Early recognition of an acute attack allows early treatment. The early symptoms which herald an acute attack are often easily recognised by those who have previously experienced an attack. When these symptoms are recognised you should stop any provoking agents such as any kind of medication. Immediate intake of sugary substances such as soft drinks or glucose tablets may help to reduce the severity of the symptoms. But you may feel too sick to do this.

Early recognition is more difficult for those people who have inherited an acute porphyria but who have never experienced an acute attack. As a consequence, there is often considerable apprehension about pains that usually turn out to be due to causes other than acute porphyria. It must be noted that people with porphyria commonly experience abdominal discomfort, just like those who do not have the condition, and a doctor will need to consider other medical conditions which may cause abdominal pain. These conditions include a range of bowel disturbances, urinary infection and sometimes other urgent medical problems such as appendicitis. In this situation, the diagnosis of acute porphyria can usually be established or excluded by testing the urine for porphobilinogen (PBG).

### Treatment of an acute attack:

As soon as an acute attack is suspected, you should contact your physician for rapid hospitalisation if the acute episode is severe.
This will allow :

- Biochemical diagnosis of the acute attack by measuring PBG in urine.
- Early start of specific treatment of the acute attack : for example, with intravenous human hemin.
- Administration of other medications to treat the various symptoms accompanying the attack. These treatments are likely to include the use of drugs to relieve pain and nausea and to provide sedation. It is also important to maintain an adequate intake of calories and this may require feeding intravenously or through a naso-gastric tube.

Human hemin helps to overcome the relative deficiency of heme in the liver and takes away the body’s desire to increase the supply of the chemicals (porphyrins and precursors) needed for heme production. Human hemin is the first choice treatment. If it cannot be obtained soon enough, large quantities of glucose, which have a similar but lesser effect, may be administered in the meantime.

## 13. SKIN PROBLEMS IN THE ACUTE PORPHYRIAS

The skin is never affected in acute intermittent porphyria. Skin problems occur in 10-20% of adults who have inherited the gene for variegate porphyria and are often their only symptom. Areas of skin exposed to sunlight, particularly the backs of the hands, face and legs, become fragile, break easily and form blisters. Broken areas may become infected, be slow to heal and leave small scars.

If you have skin problems, you should look after your skin carefully. Avoid direct sunlight as much as possible, even sunlight that has passed through window glass in your home or car. Protect your skin from sunlight by wearing light cotton gloves, long sleeves and a hat when you go out. Not everyone will find this necessary or acceptable;adjust your clothing as it suits you. Ordinary sunscreen ointments are not effective. The only ones that may help are the thick, opaque preparations with high protection factors (often containing titanium oxide) that block both UVA and UVB light. Try to protect your hands from injury. Use a silicone barrier cream and rubber gloves when working in the kitchen or elsewhere. Keep any broken or blistered skin clean by washing with water and a mild soap; avoid strong antiseptics.
Identical skin problems may occur in hereditary coproporphyria but usually only during an acute attack of porphyria and are rarely persistent.

## 14. CONCLUSION

It should never be forgotten that most people found to have an acute porphyria are able to lead a normal healthy life. All that is needed is to take the few simple measures to decrease the risk of illness that are described here. Even the few who do become ill usually make a complete recovery and have no more than one or two acute attacks in early adult life. As one grows older, the risk of an acute attack decreases, particularly after the age of forty, but it never completely disappears.

## 15. LIST OF PATIENT SUPPORT GROUPS

The below list is non exhaustive. If you know of a patient support group not listed below please contact us.

| | |
|---|---|
| **CANADA** | The Canadian Porphyria Foundation. porphyria@cpf-inc.ca<br>www.cpf-inc.ca |
| **FRANCE** | Centre Francais des Porphyries, hôpital Louis Mourier, Colombes,<br>www.porphyries.com.fr |
| **ITALY** | Associazione Malati di Porfiria (AMAPO) - Ms S. Pavia, V. Fiume Bianco, 130, 00144 Roma, Italy. crisava99@libero.it<br>Associazione Malati di Porfiria AMAPO (ONLUS)<br>Presidente S. Simona Pavia Sede : c/o Istituto S.Gallicano Via S. Gallicano, 25 CAP 00153 Roma, Italy. amapo@tiscali.it, www.amapo.it |
| **NORWAY** | www.porfyri.no |
| **SPAIN** | The Spanish Porphyria Association,<br>Mrs Rosario Fernandez<br>Arcangel San Rafael, 12, 6°, 23<br>41010 Sevilla. porfiria.es@terra.es<br>Tel/Fax : +34 95 434 00 71 |
| **SWEDEN** | The Swedish Porphyria Association,<br>Riksföreningen mot porfyrisjukdomar<br>Huddinge University Hospital C2 71,<br>SE-141 86 Stockholm, Sweden. porfyri@swipnet.se, http://home.swipnet.se/rmp |
| **SWITZERLAND** | Schweizerische Gesellschaft für erythropoietische protoporphyria. |
| **UK** | British Porphyria Association.<br>Mrs Karen Harris, 14 Mollison Rise, Gravesend, Kent DA12 4QJ.<br>Tél.: 01474 369231. kareneharris@tinyonline.co.uk |

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|---|---|
| **USA** | American Porphyria Foundation<br>P.O. Box 22712, Houston, Texas 77227.<br>www.porphyriafoundation.com |

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