# DRUG PRESCRIPTION IN PATIENTS WITH PORPHYRIA

## WHY ARE DRUGS IMPORTANT IN PORPHYRIA?

Many drugs, as a consequence of their metabolism, result in an increased requirement for haem. A common mechanism is through induction of cytochrome P450 enzymes. These are haemoproteins (proteins incorporating haem as a prosthetic group) which play an important part in drug metabolism, particularly in the liver. As a result of induction, more of these haemoproteins are synthesised, which in turn induces haem synthesis in order to provide the required haem. Increased haem synthesis then leads to accelerated porphyrin production and may result in an acute attack. Not all drugs show this property; those which do are labeled **porphyrinogenic**, are potentially **dangerous** in porphyria and must be **avoided**.

**While we take every precaution, we cannot accept any responsibility for adverse experiences arising from the use of our lists.**

See our **disclaimer**.

## THE ACUTE PORPHYRIAS

Acute attacks are seen only in the following forms of porphyria, which are known collectively as the **acute porphyrias.** Drug safety precautions are **essential** in all patients with these forms of porphyria, but are **unnecessary** in the other forms of porphyria (porphyria cutanea tarda and the erythropoietic porphyrias).

- Acute intermittent porphyria (AIP)
- Variegate porphyria (VP)
- Hereditary coproporphyria (HCP)
- ALA dehydratase deficiency porphyria.

## DIFFICULTIES IN DETERMINING PORPHYRINOGENICITY

It has become increasingly clear that it is often extremely difficult and even impossible to predict whether a particular drug will be safe in a patient with porphyria or not. Individual subjects vary in their susceptibility to drugs, even to those well-established as precipitants of the acute attack such as the barbiturates. Thus clinical experience offers only a **relative** rather than an **absolute** guide to the use of drugs in porphyria, since not infrequently patients with porphyria will safely take a drug which has proved dangerous in others, and conversely, the observation that a drug has been taken safely by a patient is **no guarantee** that it will not cause problems on a different occasion or in a different subject. Laboratory prediction of porphyrinogenicity based on animal and cell culture experiments has also proved disappointing, with poor correlation between clinical experience and the results predicted by these experiments.

It does however appear that we can, by applying some simple rules, make useful (even if not absolute) rulings on newer agents for which there is no clinical experience in porphyria. In particular, drugs whose metabolism is at most weakly associated with induction or inhibition of the cytochrome system are probably unlikely to result in the acute attack, at least in the "average" porphyric patient (this may not hold in patients with a history of very active porphyria and previous or current acute attacks, in whom extra care is needed). This allows us to continually update our lists. The NAPOS database (read *The NAPOS drug database*) is

proving very useful in this regard, and many of the recommendations on our website have been assisted by the information in that database.

## "DRUG ETIQUETTE" IN PORPHYRIA

As a result of these difficulties, we have moved away from a rigid reliance on published drug safety lists to an appreciation that the safe use of drugs is most securely based on a **culture of "safe behaviour"** with drugs, of which reference to drug safety lists constitutes just one component. The principal points to be observed are:

- People with porphyria should as far as possible avoid taking **any** drug.
- They should also **avoid recreational drugs** such as cannabis, and should limit exposure to alcohol and cigarettes.
- Drugs should only be taken where **absolutely indicated** for incontrovertible clinical indications.
- **Combinations** of drugs should be avoided since there is evidence that several drugs may act synergistically to aggravate porphyria.
- Drugs should only be prescribed after intelligent perusal of a **drug list**, looking for the **safest of the alternatives available**.

## SOME GENERAL RULES

In general, drugs applied topically (such as ointments lotions, nebulisers etc.) are safe unless there is a danger of significant systemic absorption and metabolism. Secondly, drugs which are largely excreted unchanged (without significant hepatic metabolism) are also likely to be safe.

## USING OUR DRUG LISTS

The list is presented in two ways: in alphabetical order, and then grouped together into common indications for medication, such as *Asthma*, *Diabetes* etc. You can also print out the entire list for your reference. Check back from time to time as we do update it as new information becomes available.

## RECOMMENDATIONS FOR SPECIFIC CONDITIONS

We have consolidated our recommendations for a number of conditions into specific pages which you will find under the Specific conditions item on the Prescribing menu. We will continue updating these and adding to their number in time.

## KEY TO STATUS TERMS

The following are the status terms used in the list.

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| **Use** | Likely to be safe and may be used freely. |
| **Use, but with caution** | Though safety is not established beyond doubt, the evidence suggests that the drug is unlikely to prove unsafe in practice. It is usually safe to take such a drug. |
| **Use only with extreme caution and if no alternative** | There is evidence to suggest that the drug may yet prove unsafe in practice, or grounds to suspect this may be so, or too little evidence to suggest that it may be safe. Such drugs should only be used if the expected benefits strongly outweigh the risks. If possible, use an alternative. |
| **Avoid: high risk** | There is evidence that such drugs have precipitated acute attacks in patients, or other grounds for believing that the risk of an acute attack is high. |
| **Unknown, therefore avoid** | There is too little evidence to draw a conclusion, and it is wisest to regard the drug as potentially hazardous and avoid its use. |

## THE NAPOS DRUG DATABASE

The Norwegian Porphyria Centre (NAPOS) has designed an excellent database (in English) detailing drug safety in porphyria. We are in the process of correlating our own recommendations with theirs, and we gratefully acknowledge their work. Our website contains a direct link so that you can, if you wish look up a drug on their database directly.