The
British Porphyria Association
newsletter

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Porphyrins and Porphyrias Conference 2005

The Porphyrins and Porphyrias conference in Cape Town had a very hectic schedule interspersing talks with detailed discussion of enzyme studies and mechanisms as well as clinical case histories.

The conference addressed the problems of diagnosis. This can take place using biochemical methods such as chromatography, plasma scanning and enzyme assays which is most appropriate for the diagnosis of symptomatic individuals or by DNA analysis within a family when inheritance of one of the porphyrias is suspected. It was noted that patients and clinicians of patients with porphyria often ascribe non porphyric symptoms to porphyria or overinterpret symptoms in patients with porphyria. There was a discussion of the difficult issue of how to diagnose an acute attack. Patients with acute intermittent porphyria often have constantly raised porphobilinogen (PBG) excretion making it difficult to discriminate between an acute attack and other causes of abdominal pain. Increases from an individual's baseline value may be useful but patients are rarely monitored for PBG so the final decision is often dependent on clinical judgement.

Problems in management of acute attacks including the availability of haem arginate and the recognition of complications were discussed. A serious problem that can affect some patients is that of recurrent attacks. Possible therapies included removal of precipitants, hormonal manipulation, prophylactic haem arginate therapy, metalloporphyrin therapy, liver transplantation, enzyme replacement and gene therapy. Annika Johansson from Sweden won the clinical excellence award sponsored by the Discovery Institute for her presentation "Adenoviral mediated expression of porphobilinogen deaminase in liver restores the metabolic defect in a mouse model of AIP". PBGD-deficient mice were administered with an adenoviral vector carrying mouse PBGD cDNA. Hepatic PBGD activity increased in a dose and time dependent manner. No increase in ALA or PBG was found after induction of haem synthesis in treated animals. This may suggest a future for gene therapy in AIP once a gene delivery system for humans has been perfected.

NOT all individuals with a defective porphobilinogen deaminase develop AIP symptoms. The explanation for the low clinical penetrance of this and other autosomal dominant acute porphyrias is an intriguing problem. There may be a relationship to enzyme activity and or coinheritance of low expression alleles as has been found in EPP.

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The haem pathway may become induced or there may be genes that influence susceptibility. Elisabeth Minder and X Schneider-Yin from Switzerland explored this incomplete penetrance, by generating gene expression profiles from symptomatic and asymptomatic individuals. The results suggested that various apoptosis factors were involved but due to the very small sample size these results were thought to need corroboration.

One of the difficulties for scientists and clinicians alike is that the pathogenesis of the porphyrias is incompletely understood. Symptoms may be due to haem deficiency, intraneuronal haem deficiency or toxicity and /or ALA and PBG toxicity. This also makes it difficult to predict whether certain drugs are porphyrinogenic. The drugs may induce porphyrin synthesis or interfere with porphyrin metabolism. They may increase haem degradation or utilisation. The current predictions depend on clinical experience or experience with laboratory animals or cell cultures. The other method of categorising a drug depends upon its chemical structure and metabolism. This work may be confounded by an individuals response to a particular drug. Professor Jean Charles Deybach from Paris presented details of the European Porphyria Initiative website. He stressed that treatment requires a standard approach with consensus on safe and unsafe drug lists. There are lists available on the site along with frequently asked questions for example drugs recommended for contraception, local anaesthesia, epilepsy control and pain management.

Hepatocellular carcinoma is known to be a problem for patients with acute porphyria. Two presentations were given advocating the annual screening of patients over 50 years with ultrasound scanning. Alpha fetoprotein was not found to be useful.

This is a very small selection of the 55 talks and many posters that were presented. Some topics proved controversial involving lively, truly international discussions from both the scientific and clinical worlds. Due to the rarity of the porphyrias it requires a large international conference for "porphyrinologists" to exchange views, find out the latest research and the most successful treatments. I would like to thank Peter Meissner and his conference organising team for all their hard work and for a most enjoyable conference. Written by Sharon Whatley for EPI.

National Porphyria Awareness Day 2005

This was organised by Dr Felicity Stewart, Consultant in Clinical Biochemistry at Hope Hospital, Salford (Manchester).

The morning was a series of talks, to which both BPA members and medical staff were invited, and the afternoon was for BPA members only, with visits to two labs and the chance to ask Dr Stewart questions. There were about 35 medical staff at the morning presentations and 35 from the BPA (originally 42, but a number had to drop out). This was far more than either the BPA or Dr Stewart had expected, and there was literally standing room only in the lecture theatre. It got very hot!

Dr Stewart gave a brief introduction looking at porphyria in the north-west. The most common type is PCT (1 in 20,000), which is usually not hereditary. Treatment plus changes in life-style can prevent further problems. The next most common is AIP (1 in 100,000). Only 10 to 20 % of people with the gene actually have attacks. Other types of porphyria are rarer with CEP the most severe, but fortunately the most rare. In the north-west there are about 150 newly diagnosed cases of porphyria per year.

She also gave an explanation of the relationship between the porphyrias. AIP is caused by a problem early in the production of haem, producing a build-up of ALA and PBG (the raw materials from which haem is made), which cause attacks. VP and HCP are caused by a problem further on in the "production line", due to a feedback mechanism which causes a build-up of ALA and PBG. Skin sensitivity is caused by light-sensitive porphyrins building up (those partly converted to haem).

Mr Paul Reed, from the Porphyrin Lab, then gave an explanation of the diagnosis of porphyrias and how they distinguish between the different types. This depends on the fluorescence of the different types of porphyrin (the wavelength of light they give out, when exposed to light) and which porphyrins are present in large quantities in samples. For EPP, red cell porphyrins (from the blood) fluoresce at high wavelengths. For other porphyrias, the porphyrins in blood, urine and faeces give out different wavelengths when exposed to light. For example, VP is the only one to give fluorescence in blood plasma at a particular wavelength, distinguishing it from the other acute types. We were able to see the test equipment at the afternoon visit, with some print-outs of fluorescence showing the different peaks.

Dr Lesley Rhodes then talked about the work of the photo lab. Since there are other problems causing sensitivity to light, some of the work they do helps with diagnosis. For instance, if skin exposed to visible light reacts, it is an indication of porphyria. EPP generally causes acute photosensitivity whereas the other skin porphyrias mostly cause fragile skin, with some blistering. In EPP they recommend Dundee cream, or something similar,

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which blocks visible light completely. Normal sun-creams don't block visible light. However, those with lower sensitivity can be helped by high factor creams which have a high (***) UVA rating.

Dr Anoop Varma, Consultant Neurologist, then looked at the effects of an acute attack. All medical students are taught that acute porphyria causes pain (usually abdominal), psychosis (caused by the effects on the central nervous system) and neuropathy (loss of movement or sensitivity caused by the effects on the peripheral nerves). Other indications of porphyria include hypertension (high blood pressure) and hyponatraemia (low blood salts). Unfortunately the condition is often missed, because the symptoms don't occur together. They can often be spread over several months – the pain is usually the first, with psychosis and neuropathy following. Each could be caused by other conditions., and only a long-term view will lead to correct diagnosis.

Since the neuropathy usually occurs after other symptoms, it can lead to misdiagnosis of Guillain Barre Syndrome. However, acute porphyrias often give asymmetric neuropathy (e.g. problems using only one arm) whereas GBS is symmetrical. Also, with porphyria, the loss of sensation tends to be round the "bathing-suit" area, with motor problems in the extremities, not both in the same area. (A very severe attack of porphyria may eventually cause breathing problems, when a ventilator is needed until the nerves have time to repair.) There is also a difference in the part of the nerve affected – the axon (fibre) in porphyria and the myelin (covering of the axon) in GBS. So accurate observation of symptoms and a long-term view are needed for a correct diagnosis.

Lunch was then served (free sarnies and drinks, thanks to sponsorship organised by Dr Stewart), and the BPA members were divided into two groups to visit the Porphyrin Lab and the Photo Lab. Even divided, there were more than could visit the Porphyrin Lab at once, so we had to wait our turn in a conference room nearby. Dr Stewart very kindly sat with us and answered questions from members, while we waited. One member asked about tests, as hers had come back negative, despite other symptoms of acute porphyria. Dr Stewart advised her to make sure she was tested when she became unwell, as levels of ALA and PBG can go back to normal between attacks.

The Photo Lab was able to take larger numbers so there was less of a delay there, but members still had time to ask questions.

The Open Day was very much appreciated by members, with a couple of exceptions. Mostly the speakers were very good at explaining their subject without getting so technical that only the medical staff could understand. Since it was the first time Dr Stewart had tried organising this type of event, and the first time the BPA had been involved, we felt that it had gone extremely well – though the hot weather added to the exhaustion of the organisers!

COMMITTEE CHANGES

Several changes have taken place within our committee this year. Pamela Spencer who has been a trustee and committee member since the inception of the BPA has stood down. We would like to thank her for all of the work she has done for the association over the years and especially for the use of the committee rooms at her company Clarke Steele in Cambridge.

Leigh Drake will retire as secretary, a position that she 'stepped into' last year to help us out. She is getting engaged in December and will be spending quite a bit of time abroad. We would like to thank her for the work that she has done and wish her the best of luck for a very happy future.

Sarah Pepperdine joined our committee earlier in the year and we would like to welcome her. Her own introduction can be read elsewhere in this newsletter.

WWW.buy.at/BPA

No doubt your thoughts will by now have turned towards Christmas and the inevitable task of buying presents.

Why not do it ALL on line this year. Our on line shop accessed through the above web site will give you access to many participating stores.

Retailers like Marks & Spencer, Amazon, LXdirect, Comet, John Lewis and Goldsmiths pay commission on purchases to the British Porphyria Association, making your gifts to family and friends also gifts to us!

Each retailer states how much per purchase, either in £'s or % they will donate to the BPA, so you will be able to work out exactly how much your purchase will be worth to us.

Anyone can use our Web Shop, so pass on the details to your friends, family and work colleagues, especially when sending out emails.

→MY STORY

Living with EPP – Sarah Pepperdine

When I was born back in May 1970 I was a miserable baby, being a summer baby my parents used to put me in my pram in the sunny garden little knowing that it was probably that making me miserable! No one knew what was wrong with me and why do I keep waving my arms around?! I was diagnosed as having hay-fever, which my parents thought wasn't the case but thought the doctors knew more!

When I was four I was finally given the diagnosis of having Erythropoietic Protoporphyria – a condition which even to this day I can't say, let alone spell....!

Well, what does having EPP mean to me, in a nutshell it means not being exposed to the sun. Luckily for me I live in England and we don't have all that much sun here! I am not able to go in any bright light (UV) which makes the summer the worse time of year although really anytime from March until November is difficult. I use factor 60 sun screen, an umbrella and cover up with long sleeves, wear trousers etc – which all makes me very hot and irritable, I can tell you!

When I tell people I can't go in the sun the first thing they ask is "where do you go on holiday?" I always reply, in the winter in England! But I don't really miss holidays it's simple things I miss or get annoyed at not being able to do, like being able to take my kids on summer picnics (during the day as opposed to going in the late evening or in winter!), being able to watch their sports days at school and even chatting with other mums at the school gate. Late night shopping is great during the summer for me as it means I can load and unload the car slowly rather than throwing things in the boot and rushing indoors! I suppose more people are aware that the sun is bad for everyone so it means there are items such as high factor sun creams available in high street chemists now. We also have the big shopping malls all indoors and undercover so I can still shop.....!!

When I have caught the sun I'm in a lot of pain and discomfort, my skin feels like its burning but at the same time I don't like it getting cold or too hot, anywhere I have been exposed swells up - it also zaps my energy and I feel so tired, I tend to lay down with an electric fan blowing cool air on me. My hands have toughened up over the years and they manage to cope with a bit of sun. A couple of years ago I caught the sun pretty bad in October in England and my face scabbed, leaving a few scars.

I have two children, Ryan (13) and Eloise (5) and they don't have this condition, which is great and the only time it affects them is the embarrassment of walking with me and my brolly!

I suppose over the years I have learnt to cope with this and being a person 'whose glass is _ full' I always think that there are so many other ailments and problems people have that not being able to go in the sunlight really isn't a big deal.

www.porphyria.org.uk

If you have not already visited our web site, please find time to do so. You will find links to other sites relevant to those with Porphyria and our web master regularly up dates it with news, members experiences and frequently asked questions.

We welcome suggestions for additions or improvement to the web site which can be sent by email to webmaster@porphyria.org.uk.

We would also like to hear from anyone who would like to send us their story, poems or articles about porphyria.

HELPLINE CONTACT TIMES

Would members please note that our helpline is not manned at specific times, due to work and family commitments.

As a guideline please try to phone during the following hours, when someone is most likely to be in attendance. Outside of these hours the answer machine will be in operation.

Tel: 01474 369 231

Monday	**19.30 hrs – 21.00 hrs**
Tuesday	**12.00 hrs – 14.00 hrs**
Wednesday	**Answer machine only**
Thursday	**14.00 hrs – 15.30 hrs**
Friday	**10.00 hrs – 14.00 hrs**

Weekends and Bank holiday – Answer machine:- Please leave, name, phone number, day and time of message and someone will call you back as soon as possible.

The BPA Newsletter is published by the BPA twice yearly.

Chairman: John Chamberlayne
Treasurer: Anne Newton
Secretary: Sarah Pepperdine
Patron: Prof. Timothy Cox, Prof. George Elder

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Tel: 01474 369 231 email: BPA@bodywise.go-plus.net

FUND RAISING & DONATIONS

→ We would like to express our thanks to the following for their recent fund raising efforts and everyone else who has sent in donations, not mentioned here.

→ Paul & Leilah Kelsey from Halifax who raised £456.60 by running the Leeds half marathon. They completed the course in a very respectable 2 hours 50 minutes, despite Leilah having sprained her ankle in the previous week. They would like to thank all of their family, friends and work colleagues for their support.

→ Annette Minger found a novel way to raise funds for the BPA whilst having a good evening with her friends. She held a Body Shop Party and over 19 people ordered products worth over £600 with the commission of £100 presented to the BPA. Annette gave a speech on Porphyria helping us to raise awareness amongst her friends and colleagues.

→ Garry Doughty spent months training for the London Marathon and sent us a cheque for £155 from the proceeds of his sponsorship. He completed the gruelling course in just 3 hours 47 minutes. His wife Janice is especially proud of him and would like to thank him for everything he does for her as she is the only one in the family with Porphyria.

→ We would also like to thank ALL members who have returned to us a completed Gift Aid form, allowing us to claim back 28p in the pound from donations and membership fees. If you are a tax payer, please complete and return a Gift Aid form to enable to claim this benefit.

→ This year the Inland Revenue have sent us a cheque for £470.78.

Membership/ Donation Form

BRITISH PORPHYRIA ASSOCIATION

Registered Charity No. 1089609

By making a donation to the British Porphyria Association you will know that you are making a vital contribution our work. Simply making a small donation will help us raise awareness, expand our help line or support our research.

DO YOU PAY UK TAX?
If you do, you can add 28% to the value of your gift to the British Porphyria Association at no extra cost to yourself, Simply sign and date the Gift Aid declaration and for every £1 you give, we can ask the Inland revenue to give us an extra 28p.

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☐ I would like to pay my annual membership fee of £10

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☐ I would like to pay by Standing Order (please fill in the form overleaf)
☐ I enclose a cheque made payable to the British Porphyria Association

for £ .....

STANDING ORDER

BRITISH PORPHYRIA ASSOCIATION

Please send this form to: The Treasurers, British Porphyria Association, 11 Blakehill Terrace, Undercliffe, Bradford, West Yorks, BD2 3JS

A monthly standing order or any donation you can give will make a difference.

Bank/Building Society name .....
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Please pay the British Porphyria Association the sum of £ ..... each month/quarter/year (delete as appropriate) from my account until further notice.

Account name(s) .....
Account no. ..... Sort code .....
Starting on* (date) .....

* This date must be more than one month after today's date

Signed .....
Todays date .....

This cancels all existing Standing Orders to the British Porphyria Association (please tick) ☐ yes ☐ no ☐ not applicable

GIFT AID DECLARATION

I am a UK Tax payer and would like the British Porphyria Association (Registered Charity No.1089609) to treat all donations I have made since 6th April 2000, and any future donations, as Gift Aid donations until I notify you otherwise. (we can reclaim the tax on your donations at no cost to yourself)

Signature .....

Date .....