JPAC 11-08

Joint UKBTS / NIBSC Professional Advisory Committee ([1])
Summary Sheet

1. Paper for the JPAC meeting on:	10/3/2011
2. Date submitted:	21/1/2011
3. Title (including version no.):	New DSG entry for Porphyria
4. Author(s):	SAC Care and Selection of Donors Dr Sue Barnes
5. Brief summary:	The attached paper makes recommendations for the donor selection guidance on potential donors with porphyria these were endorsed by the SAC CSD on 9/12/10
6. Action required by the Joint Professional Advisory Committee : (What do you want JPAC to do in response to this paper?) e.g. • endorse a specific recommendation • advise where there is a choice of possible actions • advise on priorities within the work plan • provide a steer on policy	Endorse recommendations
7. Any other relevant information:	

([1]) **J**oint **U**nited **K**ingdom **B**lood **T**ransfusion **S**ervices and **N**ational **I**nstitute for **B**iological **S**tandards and **C**ontrol **Professional Advisory Committee**

Recommendations on Donor Selection Guidance for Porphyria

Prepared by Dr S M Barnes Chair SAC CSD

1 Remit

The remit of this paper was to prepare guidance on Porphyria in light of a number of recent requests for guidance

2 Summary of recommendations

New guidance for patients with porphyria is recommended:

Obligatory
Must not donate if:

Suffers form porphyria

Discretionary

If the potential donor suffers from an Acute porphyria, Acute intermittent porphyria (AIP), Varigate Porphyria (VP) or Hereditary Coproporphyria (HCP)and it is 12 moths since their last acute attack and they have no skin lesions, accept.

See if Relevant
Hepatitis

Additional Information
Acute porphyrias (AIP, VP and HCP) may be associated with skin lesions and raised blood porphyrins independently of acute attacks. Theoretically the recipient of the blood could develop skin lesions we therefore exclude anyone with active skin lesions.

Porphyria Cutanea Tarda (PCT) is almost always an aquired condition associated with underlying liver disease, usually hepatitis often of viral or unknown origin. These patients the patient is often treated by venesection, however because of the risk of transmission of the agent that caused the condition the blood is not suitable for transmission.

Erythropoietic Protoporphyia (EPP) and Congenital Erythropoietic Porphyria (CEP) Often the patient is anaemic because of the condition, and in these conditions there are porphyrins in the red cells and red cell life time is reduced so the blood is not suitable for donation

3 Background

The current guidance in DSG 203 does not contain any advice on Porphyria and BSQR 2005 is silent on the condition. Porphyrias are a group of inherited or acquired disorders of certain enzymes in the heme bio-synthetic pathway (also called porphyrin pathway). They are broadly classified as acute (hepatic) porphyrias and cutaneous (erythropoietic) porphyrias, based on the site of the overproduction and accumulation of the porphyrins (or their chemical precursors). They manifest with either neurological complications or skin problems (or occasionally both).

The acute or hepatic porphyrias are characterized by acute neurological attacks (seizures, psychosis, extreme back and abdominal pain and an acute polyneuropathy), while the erythropoietic forms present with skin problems, usually a light-sensitive blistering rash and increased hair growth. Variegate porphyria (VP), which results from a partial deficiency in PROTO oxidase, manifests itself with skin lesions similar to those of porphyria cutanea tarda combined with acute neurologic attacks. All other porphyrias are either skin- or nerve-predominant.

Patients with acute porphyria (AIP, HCP, VP) are at increased risk over their life for hepatocellular carcinoma (primary liver cancer) and may require monitoring. Other typical risk factors for liver cancer need not be present.

The cutaneous, or erythropoietic, porphyrias primarily affect the skin, causing photosensitivity (photodermatitis), blisters, necrosis of the skin and gums, itching, and swelling, and increased hair growth on areas such as the forehead. Often there is no abdominal pain, distinguishing it from other porphyrias. In some forms of porphyria, accumulated heme precursors excreted in the urine may cause various changes in color, after exposure to sunlight, to a dark reddish or dark brown color. Even a purple hue or red urine may be seen.

In humans, porphyrins are the main precursors of heme, an essential constituent of hemoglobin, myoglobin, catalase, peroxidase, respiratory and P450 liver cytochromes. Deficiency in the enzymes of the porphyrin pathway leads to insufficient production of heme. Heme function plays a central role in cellular metabolism. This is not the main problem in the porphyrias; most heme synthesis enzymes—even dysfunctional enzymes—have enough residual activity to assist in heme biosynthesis. The principal problem in these deficiencies is the accumulation of porphyrins, the heme precursors, which are toxic to tissue in high concentrations. The chemical properties of these intermediates determine the location of accumulation, whether they induce photosensitivity, and whether the intermediate is excreted (in the urine or feces).

There are 6 ‘common’ subtypes of porphyria in adults; these depend on what enzyme is deficient.

Enzyme	Location of enzyme	Associated porphyria	Type of porphyria	Inheritance	Symptoms
hydroxymethylbilane (HMB) synthase (or	Cytosol	Acute intermittent	Hepatic	Autosomal dominant	Periodic abdominal pain, peripheral

PBG deaminase)		porphyria (AIP)			neuropathy, psychiatric disorders,
uroporphyrinogen (URO) synthase	Cytosol	Congenital erythropoietic porphyria (CEP)	Erythropoietic	Autosomal recessive	Severe photosensitivity with erythema, swelling and blistering. Hemolytic anemia, splenomegaly
uroporphyrinogen (URO) decarboxylase	Cytosol	Porphyria cutanea tarda (PCT)	Hepatic	Aquired or Autosomal dominant	Photosensitivity with vesicles and bullae
coproporphyrinogen (COPRO) oxidase	Mitochondrion	Hereditary coproporphyria (HCP)	Hepatic	Autosomal dominant o	Photosensitivity, neurologic symptoms, colic
protoporphyrinogen (PROTO) oxidase	Mitochondrion	Variegate porphyria (VP)	Mixed	Autosomal dominant	Photosensitivity, neurologic symptoms, developmental delay
Ferrochelatase	Mitochondrion	Erythropoietic protoporphyria (EPP)	Erythropoietic	Autosomal dominant	Photosensitivity with skin lesions. Gallstones, mild liver dysfunction

Expert advice has been sought from Professor Cox Professor of Medicine, Dr Patrick Deegan Consultant Physician with a special interest in metabolic disorders and Dr Penelope Stein, all of Department of Medicine, University of Cambridge, Addenbrookes on the acceptability of potential donors with the various forms of porphyria being accepted as blood donors. They delivered the following advice:

> ‘Acute porphyrias (Acute Intermittent Porphyria AIP, Variegate Porphyria VP, Hereditary Coproporphyria HCP)- This group are probably safe to donate if they have not had an acute attack during the past year. There is just one potential problem in relation to VP and HCP as these porphyrias (but not AIP) may be associated with skin lesions and raised blood porphyrins independently of acute attacks. Theoretically the recipient of the blood could develop skin lesions, however there would be a significant dilution effect. Also, the porphyrins in the donor blood would be in the plasma, not the red cells. The red cells are normal in VP and HCP. I'm inclined to think the risk is negligible, but you could decide to exclude anyone with active skin lesions.
>
> Porphyria Cutanea Tarda (PCT) - We all agree that it would be risky to accept their blood for donation even if their skin disease is in remission, as this is almost always an aquired condition associated with underlying liver disease.

22/12/2010 S M Barnes

Erythropoietic Protoporphyia (EPP) - There are porphyrins in the red cells and red cell life time is reduced so not suitable for donation.

Congenital Erythropoietic Porphyria (CEP) - Again there are porphyins in the red cells so not suitable. In any case these patients won't present as donors, and frequently need blood transfusions themselves.'

Review of international guidance reveals that in the US donors with Porphyria Cutanea Tarda are deferred by the New York Blood Centres, most other services have not yet considered the condition, nor have other nations.

On this basis, I recommend changing the Donor Selection Guidance as outlined above.

S M Barnes 10/11/10

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Date of publication:	Implementation:

Change Notification UK National Blood Services No. - 2011

Applies to Whole Blood and Component Donor Selection Guidelines only.

Porphyria

Obligatory

Must not donate if:
Suffers from porphyria

Discretionary
If the potential donor suffers from Acute Porphyria, Acute Intermittent Porphyria (AIP), Varigate Porphyria (VP) or Hereditary Coproporphyria (HCP), it is 12 months or more since their last acute attack and they have no current skin lesions, accept.

See if Relevant
Hepatitis

Additional Information
Acute porphyrias (AIP, VP and HCP) may be associated with skin lesions and raised blood porphyrins independently of acute attacks. Theoretically the recipient of the blood could develop skin lesions we therefore exclude anyone with active skin lesions.

Porphyria Cutanea Tarda (PCT) is almost always an acquired condition associated with underlying liver disease, usually hepatitis of viral or unknown origin. These patients are often treated by venesection, however because of the risk of transmission of the agent that caused the condition the blood is not suitable for transfusion.

With Erythropoietic Protoporphyria (EPP) and Congenital Erythropoietic Porphyria (CEP) the patient is often anaemic because of the condition. Also in these conditions there are porphyrins in the red cells and red cell life span is reduced so the blood is not suitable for donation.

Update Information
This entry was last updated in:
DSG-WB Edition 203, Release *?????*.

Reason for Change
This is a new entry.

Further Information
The supporting paper, recommendations on Donor Selection Guidance for Porphyria, leading to this Change Notification can be found in the Document library/Supporting Papers of the JPAC website: http://www.transfusion guidelines.org.uk

Donor Information
If you wish to obtain more information regarding a personal medical issue please contact your National Help Line.

Please do not contact this web site for personal medical queries, as we are not in a position to provide individual answers.