FOCUS ON RARE DISEASES

The National Society for Phenylketonuria

Suzanne Ford

Dr Michelle Muscat interviews SUZANNE FORD, the Society Dietitian at The National Society for Phenylketonuria [NSPKU], in the UK.

Phenylketonuria (PKU) is an autosomal recessive condition. The amino acid phenylalanine is usually metabolized to tyrosine by the enzyme phenylalanine hydroxylase [PAH] also requiring a cofactor named tetrahydrobiopterin. In phenylketonuria, phenylalanine is not metabolized to tyrosine. Phenylalanine is an essential aromatic amino acid. High phenylalanine levels in patients with PKU can result in neurotoxicity. The mainstay of treatment is protein restriction in the diet.

HOW DID YOU BECOME INVOLVED WITH THE NSPKU?

I work as a dietitian in the NHS, supporting adults with PKU and have done this since 2009; I knew the NSPKU provided other services and support. I had already spoken at the society's conference and stood in for the society dietitian at another event, so when the post became vacant I was pleased to have this great opportunity.

CAN YOU TELL ME MORE ABOUT THE ORIGINS OF THE SOCIETY?

The NSPKU was founded in 1973 by Brian and Sylvia Smith who put an announcement out on national radio to appeal for interest in meeting other families affected by the disorder – they also wrote to dietitians and other families that they had addresses for. There was a preliminary meeting in a community centre in November in 1973 and then the first General Meeting in April 1974 in Blackpool. In 1975 a Medical Advisory Panel had been added and in 1983 the society employed its first dietitian, and had an internet presence by 1996.

DO YOU BELIEVE THE AWARENESS OF PHENYLKETONURIA HAS CHANGED ALONG THE YEARS?

The families who live with PKU have always been instrumental in calmly explaining what PKU is to others who need to know. In the UK, recently families and people living with PKU have surpassed themselves by writing to MPs and alerting them to the life challenges this disorder brings to those affected. These MPs have held debates in parliament – filmed on parliamentlive.tv; also, MPs tried the "PKU Diet-for-a-Day" challenge, which they publicised on social media. The diet challenge, restricting the diet to ≤10g of protein in one whole day, happened on International PKU Awareness Day - on 28 June 2018 - and was the subject MPs were most tweeting about on that day.

WHAT WAS YOUR MOST REWARDING ACHIEVEMENT?

I was pleased to appear on the BBC news channel to explain PKU and the way that the pharmacological treatment sapropterin (also called BH_4, tetrahydrobiopterin, trade name Kuvan®) could change lives for responders who have PKU. Tetrahydrobiopterin is an enzyme chaperone for the defective enzyme in PKU – PAH - and thus it can remove the significant burden of dietary treatment in responders. The BBC news item was following the report of a successful high court case for a small boy with PKU who is autistic and is now allowed to have BH_4 funded by NHS England.

A recent team effort that NSPKU volunteers and I undertook has been the analysis of the biggest PKU experiences survey done so far in the world; the survey was completed online by people living with PKU in the UK. We have now published the survey results in two papers in *Molecular Genetics and Metabolism Reports*. The widespread nature of difficulties was still a surprise to me and the experiences of women was shocking. Women felt frightened by messages about the dangers of unplanned pregnancies (phenylalanine is teratogenic); the burden of pregnancy is high, and the difficulty of self-care and PKU treatment management in combination with motherhood is a significant challenge.

CAN YOU DISCUSS THE EVENTS WHICH YOU ORGANISE AND HOW DO YOU SECURE FUNDING? HOW IS THE ASSOCIATION INVOLVED IN RESEARCH?

The NSPKU has an annual weekend conference for families, day-long educational events, health care professional meetings and training sessions. We rely on our community for fundraising: people running ultra-marathons, holding

book sales and fundraising "extravaganzas" as well as regular donations from funerals, bake sales, prize raffles, collection tubs and many other efforts, events and endeavours.

Each year the NPSKU sponsors research – we have a grant fund offering two grants up to £10,000 annually, which are awarded following assessment by our Medical Advisory Panel.

CAN YOU EXPLAIN FURTHER ABOUT POSSIBLE MEDICAL ADVANCEMENTS ON THE HORIZON YOU ARE PERSONALLY EXCITED ABOUT?

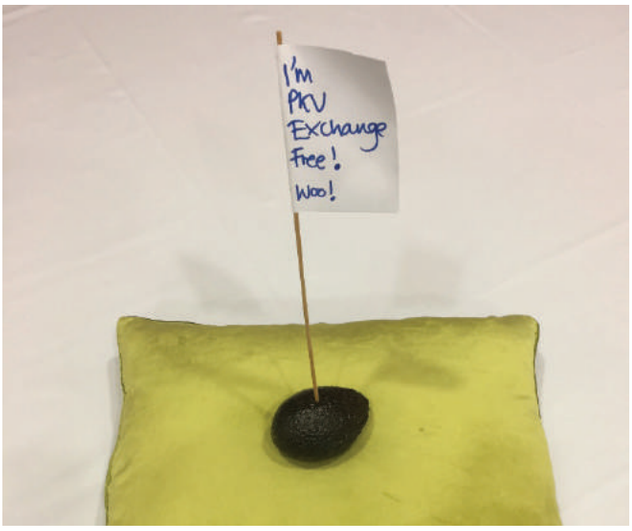
The drug treatment for PKU which is potentially nearest to being available in England is the above-mentioned BH_4 – however, we estimate only 30% of people with PKU in the UK will respond to BH_4. Pegvaliase (currently available in the US), is an enzyme substitution therapy for PKU which is injectable, and is only suitable for adults due to immunology effects.

The most exciting treatment in my opinion is a genetically engineered probiotic treatment which has successfully been through mice trials. The bacteria *Lactobacillus reuteri* was given a phenylalanine lyase gene from another bacteria, *Anabaena variabilis.* PKU mice had reduced blood phenylalanine levels after 3-4 days of treatment with the genetically modified probiotic. This seems like it would be a potentially effective treatment. The enzyme Phenylalanine lyase does the same job as the PAH which is impaired in PKU.

WHAT DO YOU ENVISAGE IN THE FUTURE FOR THE NSPKU?

The key achievement for us will be when everyone living with PKU in the UK is receiving PKU treatment to the standards outlined in the European Guidelines for Diagnosis and Management of PKU (published in brief in *The Lancet Diabetes and Endocrinology* and also in full in the *Orphanet Journal of Rare Diseases*, both in 2017). One of the many recommendations includes metabolic specialist input for people with PKU who have, in the past, been discharged from metabolic clinics, or have discontinued diet; we should be supporting them to re-access treatment. However, we don't necessarily know where these "lost to follow-up" patients are in the UK, it's possible they are in the community experiencing adverse clinical outcomes of untreated PKU. There are many challenges ahead.

More information may be found on the website: www.nspku.org/



NSPKU takes food for Phenylalanine analysis each year - Avocado after Phenylalanine Analysis

I WILL READ THE SYNAPSE JOURNAL BECAUSE...

This is the first time I encountered this publication… having gone through it, I must say that it's a concise, relevant and informative read!

In very challenging winter conditions, Andrew Tasker and friends ascend Ben Nevis, Britain's highest peak, raising £3.5k for NSPKU, Andrew has a 4 year old son with PKU