

Welcome to

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of NSPKU

Programme Information & Abstracts

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Research and Developments in PKU

Maureen Cleary MB, ChB, MD, MRCP

Consultant Paediatrician with special interest in metabolic disease.

Royal Manchester Children's Hospital

There are several areas of interesting research and development in PKU. These will be discussed by considering the following different areas of research:

- a) Developments in dietary treatment: The addition of long chain polyunsaturated fats to the amino acid supplement in PKU. The PKU diet is low on animal fats and therefore PKU children have lower levels of some important long chain fatty acids. There are several studies where the PKU amino acid mixture has been supplemented with long chain polyunsaturated fats.
- b) Measurement of brain phenylalanine using magnetic resonance spectroscopy. It is now recognized that the brain level of phenylalanine is different from the blood level. Some studies suggest that supplementing large neutral amino acids alone can alter brain phenylalanine level.
- c) The use of ammonia lyase capsules as alternative treatment for PKU. This topic will be updated with any new developments.
- d) Home monitoring for PKU. Although not yet available there are attempts at developing a home monitoring system for PKU where individuals with PKU or their parents would check the blood level at home and make the appropriate dietary changes. The extent of current research in this field will be discussed.

Genetics & PKU

Linda Tyfield, Southmead Hospital,
Bristol

The term Phenylketonuria or PKU is a biochemical description of a condition defined by phenylketones in the urine and high levels of phenylalanine in the blood (hyperphenylalaninaemia). An understanding of a basic level of biology would probably lead one to conclude that these biochemical effects arise from a defect in metabolism – a block somewhere that causes a damming effect and a spilling over of unwanted products into the urine. The word alone, however, does not hint at the different degrees of severity of the disorder or, indeed, at how any single affected individual has this disorder – i.e. that it is not acquired like an infection but inherited through the genetic material passed on from parents to offspring.

Genetic analysis – examining the single bases that constitute the gene – has provided some insight into why there are different degrees of severity of the condition. More than 400 different mutations have been described worldwide in the gene that is involved with PKU and although a few mutations are common, most are rare. Some are known to result in a more severe PKU whereas others are always associated with a mild form of the condition in which little dietary restriction of phenylalanine is required to maintain normal growth and development. Through mutation analysis it has been possible to trace the origins of the disease in different populations and to trace the migration of families through different geographical areas.

In this talk I will put 'genetic travel' into a perspective of space travel to illustrate the depths to which we travel inside the human cell in order to study individual genes. I will describe how different mutations have arisen independently in different parts of the world and I will describe some unusual mutations that we have characterised recently in the UK population. I will show how computer modelling of protein structure is used to explore the effects of single base changes in the DNA.

Diet, Fats and PKU

MacDonald A, Daly A, Asplin D, Chakrapani A, Rylance G, Birmingham Children's Hospital, Steelhouse Lane, Birmingham, B4 6NH.

What are essential fatty acids?

Fatty acids are the building blocks of fats. The body can make some of the fatty acids it needs but there are two essential fatty acids, which cannot be made in the body. These are called **linoleic** (omega -6 family) and **alpha-linolenic acid** (omega -3 family). Humans have the ability to convert these fatty acids to other important longer chain fatty acids. **Linoleic acid** is converted to arachidonic acid and remains in the omega -6 family. **Alpha-linolenic acid** is converted to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and remains in the omega -3 family.

What do essential fatty acids do?

Essential fatty acids are important in the normal functioning of all tissues of the body. Particularly:-

- The formation of healthy cell membranes.
- The proper development and functioning of the brain and nervous system.
- The production of hormone like substances called eicosanoids. (These chemicals regulate numerous body functions including blood pressure, blood viscosity, and immune responses).

Which foods do these fatty acids come from?

The best sources of essential fatty acids are plants on land and in the sea.

- **Linoleic acid** (omega -6 family) is found in seeds, nuts, grains and legumes. Good sources are corn oil, safflower oil, soybean oil, sunflower seed oil and peanut oil. Arachidonic acid comes from animal fats.

- **Alpha-linolenic acid** is found in the green leaves of plants, including algae and in selected seeds, nuts and legumes. Flax, canola, walnut oil and soy oil are all sources of this fatty acid. The only sources of EPA and DHA are fish and shellfish.

The balance or ratio of omega 3 to omega 6 fatty acids is just as important as their quantity in the diet.

Do people with PKU get enough essential fatty acids in the right balance?

There is evidence to show that people with PKU probably get enough **linoleic acid**. However, the balance between the intake of **linoleic** and **alpha-linolenic acid** may not be optimal i.e. people get plenty of **linoleic acid** but smaller amounts of **alpha-linolenic acid**. This may compromise the conversion of **alpha-linolenic acid** to the longer chain fatty acid EPA. In addition, the sources of the longer chain fatty acids e.g. EPA and DHA, are limited in low phenylalanine diets. There have now been a few studies, which show that the blood level of DHA is low in PKU.

How can we give more essential fatty acids in the right balance?

Traditionally protein substitutes in the UK have not contained fat. However, a protein substitute has now been introduced that contains both **linoleic acid** and **alpha-linolenic acid** in the recommended proportions. This is called Minaphlex (SHS). It is designed for children between 1-10 years of age. An international study (including patients from Manchester and Birmingham) showed that children who took the protein substitute with added essential fatty acids had better blood levels of both **alpha-linolenic acid** and DHA levels. It is hoped more protein substitutes will contain essential fatty acids in the future. A particularly useful source of essential fatty acids is walnut oil and this can be easily added to salad dressings.

Conclusion

In the UK, there are no current recommendations about adding essential fatty acids, particularly **alpha-linolenic acid**, to the diet. However, with increasing knowledge, this is likely to become a more prominent issue in the near future.

Life with PKU

Katie Stevens

I'm Katie Stevens and I'm 24 years old. I have been on the Low Phenylalanine diet to varying degrees for my whole life. I am here from Australia on a working holiday for approximately two years.

I grew up in Sydney and was treated at the Royal Alexandra Hospital for Children. As I was diagnosed in the late seventies information about PKU and its treatment was relatively new and continually changing.

I was the first PKU patient that my doctor at the children's hospital had treated so he was learning at the same time we were. As I was growing up I was always promised that I could stop the diet "in a few years" but as more research came to hand I ended up staying on the diet.

Growing up on a special diet had bad points but it also had some very good points. Also during my lifetime I have seen many changes and advancements in the treatment of PKU.

When deciding what to do with my future my experiences growing up with PKU helped me decide what to do. I remembered seeing the dietitian at clinic and they would always suggest new things I could try which was always important when your diet is limited. I like the way that diet can have such a big influence on so many conditions as well as PKU. I thought being a dietitian would be quite interesting and I also thought that I might be able to empathise with people on special diets.

Having PKU has not stopped me from travelling. Sometimes it has been hard but also it has helped me to do more with my diet. I have been to the UK as an exchange student after school as well as travelling to Thailand with university. I have travelled around a lot of Europe and have more trips planned for the rest of this year.

This year I am living and working in the UK. I am currently doing locum work as a basic grade dietitian. Whilst I am over here I am hoping to expand my general dietetic experience but also find out

more about PKU. Also I am here to do some more travelling as I mentioned earlier.

While I am here I would like to get some experience with the other side of PKU, the side of the dietitian rather than the patient.

My ambitions when I return to Australia are to work in paediatric nutrition and particularly inborn errors of metabolism. Also I have an interest in working in sports nutrition. I am also planning to visit the areas of my home and the rest of the world that I have not yet had time to explore.

Towards PKU Independence

Carol Ferguson, Senior Dietitian
Newcastle General Hospital

The Medical Advisory Panel (MAP) of the National Society for Phenylketonuria is aware that a significant number of PKUs reach adulthood without a firm understanding of PKU. Some adult PKUs have difficulty managing their PKU whilst busy with their work and social life.

In Great Britain we believe that “Diet for Life” is the treatment of choice for PKUs.

MAP members have therefore decided to develop strategies to help PKUs, of school age, gain a better understanding of PKU and to learn how to look after their PKU. If this can be achieved, then the adult PKUs will have a better chance of successfully continuing their PKU diet when living independent adult lives.

We have recently undertaken a survey in 3 PKU centers to assess the knowledge of PKU children about their condition and its management. We also found out how much of the PKU management the youngsters were themselves involved in. The PKU centres surveyed were Birmingham, Manchester and Newcastle. Young people (7–16 years) were surveyed.

I will explore some of the findings of this survey.

Following on from the survey we have set down a number of PKU self-management objectives for 7-11 year olds and 11–15 year olds. We envisage the objectives being used as goals which each PKU would work towards over a period of years.

We are now beginning the process of devising teaching aids/strategies that will help the PKUs achieve the various objectives with ease.

We hope that once the material has been developed and piloted it will be of help to PKU centers and PKU families. If successful, more PKU youngsters will develop self-management skills and the ability to cope with the difficulties associated with being ‘different’.

Healthy Emotional Development – How hard is that?

Dr S.E. Wressell

Consultant Child and Adolescent Psychiatrist
Flemming Nuffield Unit, Newcastle

Growing up is not easy. Children face new challenges at each stage of their development. At home, at school and with friends there are different social, emotional and psychological phases to negotiate. Growing up with a medical condition can make this more complicated, but children often surprise adults with their resilience and coping strategies. The talk will follow a child's emotional development from infancy to adolescence and highlight ways of building on the child's strengths to achieve good emotional health.

Developing an Information Pack for Young People and Adults with PKU

Susan Durham-Shearer, Maggie Lilburn and Philip Lee
The Charles Dent Metabolic Unit, National Hospital for Neurology and
Neurosurgery UCLH NHS Trust, Queen Square London, UK.

Current recommendations suggest that people with PKU should stay on low phenylalanine diet long-term (1). There is now a “first generation” of adults remaining on diet or returning to diet after a break of perhaps several years. The need for specific services for adolescent and adult PKU patients has been recognised (1), however there is still a great shortage of both medical and written resources for this patient group.

In May 2000 a research project was started at the UCLH Metabolic Unit to produce an information pack designed to address the needs of adult PKU patients. A questionnaire and knowledge test was sent out to 177 patients attending the clinic. This was to gather information such as details of current dietary regime, personal experiences of dealing with PKU and suggestions for resource pack content.

72 patients both on and off diet completed the questionnaire. The most popular topics people wanted to read about in the pack were evidence for staying on PKU diet; guidance on dealing with healthcare professionals; explaining PKU to other people and “life-stories” from other PKU patients.

This information was used to design a small “filofax style” information folder covering a wide variety of topics. A separate pack for storing blood-test results and equipment was also created.

The pack will be audited using a sample group of patients to see if it has any effect on the management of their PKU.

The pack should be available to all users of the UCLH Metabolic Clinic after May 2002.

Reference

1. Report of Medical Research Council Working Party of Phenylketonuria (1993). Recommendation on the Dietary Management of Phenylketonuria. Archives of Disease in Childhood, Vol. 68, No 3 pp426-427.



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