NHD in practice

FACT FILE

NEW CENTRE PULLOUT FEATURE

PHENYLKETONURIA (PKU)

WHAT IS PKU?

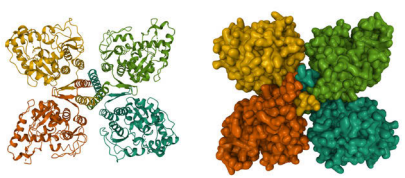
PKU is a rare inherited metabolic disorder (IMD). A metabolic disorder occurs when abnormal chemical reactions in the body disrupt the process of metabolism. There are different groups of metabolic disorders. Some affect the breakdown of amino acids, carbohydrates or lipids, for example.[1-3] PKU is an amino acid disorder. People with PKU have problems breaking down an amino acid called phenylalanine (Phe) from the protein in the food they eat.

WHAT CAUSES PKU?

Protein is made up of 20 amino acids (building blocks). Some of these amino acids are essential and cannot be made in the body, so come from the foods we eat. In order for the body to use protein for energy from the food we eat, it is broken down into these amino acids and certain enzymes then make changes to them so the body can use them.[6]

PKU occurs when an enzyme called phenylalanine hydroxylase (PAH) is either missing or not working properly. Enzymes help chemical reactions in the body; the job of PAH is to chemically convert one of the essential amino acids coming from food – phenylalanine (Phe – pronounced 'fee') – into tyrosine (Tyr), which is a non-essential amino acid, i.e. one that is made in the body and can also be found in foods. Tyr is important for the production of several brain chemicals called neurotransmitters and so is essential for cognitive function and memory.[7]

In people with PKU, the chemical change from Phe into Tyr does not occur and Phe builds up in the blood, potentially causing a variety of lifelong symptoms.



AMINO ACID DISORDERS

These disorders are inherited conditions caused by enzymes that don't work properly. A number of different enzymes are needed to process amino acids for use by the body. Because of missing enzymes or enzymes that don't work as they should, people with amino acid disorders cannot process certain amino acids, which then, along with other toxic substances, build up in the body and cause problems.[4]

REFERENCES

Please visit: www.NHDmag.co.uk/article-references.html

ESSENTIAL RESOURCES

The complete European guidelines on phenylketonuria: diagnosis and treatment. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5639803

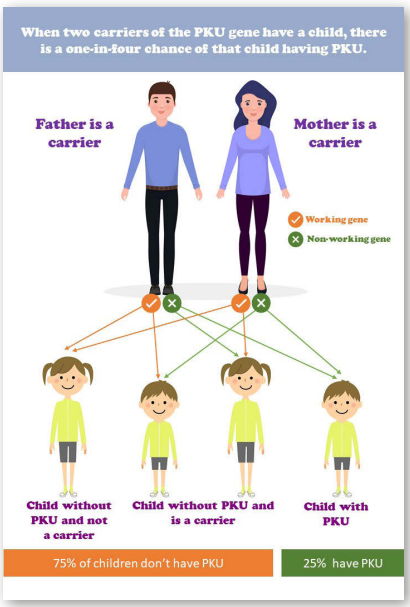
National Society for Phenylketonuria (NSPKU). https://www.nspku.org/

Sapropterin for treating hyperphenylalaninaemia in phenylketonuria. Technology appraisal guidance [TA729] (Published: 22nd Sept 2021). https://www.nice.org.uk/guidance/TA729/chapter/1-Recommendations

Examples of amino acid disorders include:

- Phenylketonuria
- Tyrosinemia
- Homocystinuria
- Nonketotic hyperglycinemia
- Maple syrup urine disease

The symptoms and treatments vary between different amino acid disorders. They can also vary from person to person with the same amino acid disorder. Amino acid disorders are inherited in an 'autosomal recessive' manner and affect both males and females.[4]

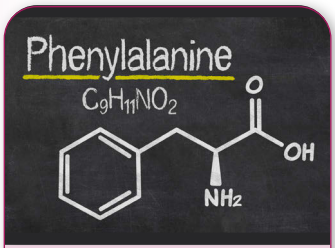


AUTOSOMAL RECESSIVE INHERITANCE

Autosomal recessive is one of several ways that a trait, disorder, or disease can be passed down through families. An autosomal recessive disorder means two copies of an abnormal gene must be present in order for the disease or trait to develop.[5] Genes come in pairs. One gene in each pair comes from the mother and the other gene comes from the father. Recessive inheritance means both genes in a pair must be abnormal to cause disease. People with only one defective gene in the pair are called carriers. These people are most often not affected with the condition. However, they can pass the abnormal gene to their children.

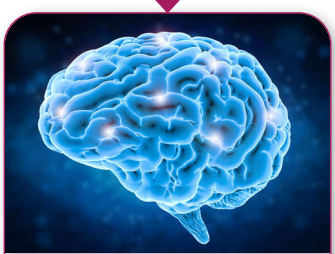
Whilst everyone has a pair of genes that make the PAH enzyme, in children with PKU, neither of these genes works correctly. These children inherit one non-working PKU gene from each parent. Parents of children with PKU are carriers of the condition. When both parents are carriers, in each pregnancy the risk to the baby is as follows:[1]

- 25% chance (1 in 4) of PKU
- 50% chance (1 in 2) for the baby to be a carrier of PKU



The essential amino acid phenylalanine (Phe) is found in most protein-containing foods.

The enzyme phenylalanine hydroxylase (PAH) converts Phe into tyrosine (Tyr).



Tyr is an essential component for the production of several brain chemicals.

In PKU, PAH is missing or faulty so that Phe can't be processed. Blood Phe increases to neurotoxic levels as Phe cannot be converted into Tyr.

NEWBORN SCREENING

Every baby in the UK is offered newborn blood spot screening, also known as the heel prick test, ideally when they're five days old. The midwife pricks the baby's heel and collects four drops of blood onto a blood spot card. The heel prick test screens for nine rare but serious conditions, including PKU.[8] Only around 1 in 10,000 babies born in the UK has PKU. Around 1 in 50 adults are carriers.[3]

WHAT ARE THE SYMPTOMS OF UNTREATED PKU?

The first symptoms are usually seen around six months of age. Untreated infants may be late in learning to sit, crawl and stand. They may pay less attention to things around them. A child with PKU who doesn't get treatment will become intellectually disabled. Some of the things caused by untreated PKU include:

- Brain damage
- Behaviour problems (such as hitting and biting)
- Hyperactivity
- Restlessness or irritable mood
- Seizures
- Eczema
- Body odour
- Light hair and skin

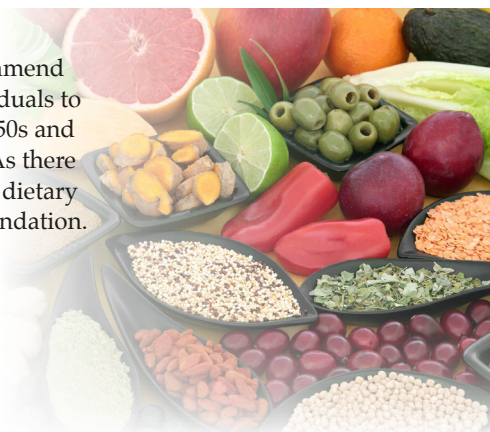
WHAT IS THE TREATMENT FOR PKU?

Phe is found in all protein-containing foods, such as meat and dairy. In order to manage PKU, all protein foods must be restricted and a low-Phe (low-protein) diet must be followed, referred to as the 'Diet for Life'.[9] As Phe helps with growth, development and tissue repair, it is important that those with PKU get some Phe, but not so much that it becomes harmful.

THE DIET FOR LIFE

The 2017 European Guidelines on PKU management recommend 'treatment for life' for people with PKU.[10] The oldest individuals to be diagnosed through newborn screening are now in their 50s and the impact of high levels of Phe on ageing are not known. As there is currently no strong evidence that it is safe to discontinue dietary treatment in adults, treatment for life remains the recommendation. Treatment for life usually means diet for life:[9-11]

- Limited high-protein foods
- Measured amounts of Phe-containing foods
- A protein substitute
- Low-protein foods
- Avoid aspartame



Newborns

Breast milk provides limited but essential Phe for normal growth. Babies diagnosed with PKU will be given a special Phe-free formula until the levels of Phe fall back to normal (usually within a few days). Once the levels of Phe are under control, a small amount of Phe-free formula is given before a breastfeed to restrict the amount of breast milk taken by the baby. If the mum is not breastfeeding, a restricted amount of standard baby formula will be given along with the Phe-free formula to provide the limited Phe essential for normal growth.

Weaning

Starting a baby with PKU on solid foods is at around six months of age, the same as babies without PKU. Foods will initially be Phe-free with a very low-protein/Phe content. This helps the child to develop a healthy eating pattern with a variety of fresh foods included in the diet. A second-stage protein substitute can be introduced.

Adolescents and adults

Regular monitoring of Phe levels will occur throughout childhood and adulthood, including frequent blood tests to check Phe, height and weight measurements, and developmental checks.

Everyone with PKU needs treatment.

PROTEIN SUBSTITUTES

When following a low-protein diet, taking protein substitutes is essential to ensure that Phe levels are kept within the recommended range. A protein substitute is a specially made medical supplement, which can come in various formats like a drink, a gel, or tablets. Protein substitutes contain minimal or no Phe but all the other required amino acids are included. Most protein substitutes also contain vitamins, minerals and other important nutrients, and as a crucial part of the PKU diet, they must be taken regularly and evenly spread over the day to help keep Phe levels steady and maintain lean body mass.

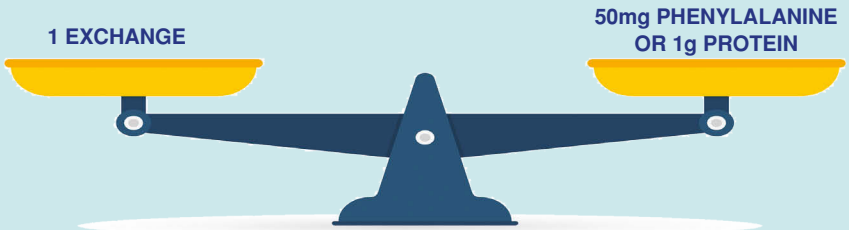
LOW-PROTEIN FOODS ON PRESCRIPTION

The degree of protein restriction in the diet of people with PKU in the UK is on average 10g protein per day.[2] This means that many food 'staples' are excluded from the diet and individuals need low-protein foods on prescription, such as flour, bread, pasta and milk substitutes.

EXCHANGES[1]

Certain foods contain small amounts of protein, such as potatoes, peas, rice, chips and some cereals, and can be eaten in measured amounts.

The measure is called an 'exchange' and the quantities allowed will vary from person to person and from time to time in the same person.



Exchanges are spread out between the day's meals to provide small amounts of essential Phe.

SAPROPTERIN

In August 2021, Sapropterin was approved by NICE as an option for treating people with PKU.[12] Sapropterin is now available in England for everyone with PKU, of all ages, who is shown to respond to the drug. The recommended dose is 10mg/kg, only using a higher dose if target blood Phe levels cannot be achieved at 10mg/kg.

HOW DOES SAPROPTERIN WORK?

Sapropterin stimulates the activity of residual PAH and helps restore enzyme action, thereby reducing blood Phe levels.