

Dietary treatment for children and adults with inherited metabolic disorders: Focus on phenylketonuria

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THE NATIONAL CENTRE FOR INHERITED METABOLIC DISORDERS is based at the Children's University Hospital, Temple Street, Dublin and treats both children and adults with Inherited metabolic disorders. Treatment for these conditions is lifelong. The most commonly treated condition is phenylketonuria (PKU). The national newborn screening programme was first introduced in Ireland in February 1966, with screening for phenylketonuria following the development of the Guthrie screening test. This is commonly known as the heel prick test. Ireland was one of the first countries in the world to have a national screening programme.

Inherited metabolic disorders, which can be treated mainly through dietary interventions, can be divided into three main groups:

- *Amino acid disorders*: Phenylketonuria, maple syrup urine disease and homocystinuria
- *Disorders of carbohydrate metabolism*: Classical galactosaemia and glycogen storage disease
- *Fatty acid disorders*: Medium chain acyl- coenzyme A dehydrogenase.

These conditions are as a result of a deficiency of an enzyme necessary in the degradation of amino acids, carbohydrates or fatty acids.

Six medical conditions are screened for using the Guthrie screening test as listed below. The first four listed are metabolic disorders:

- PKU
- Homocystinuria
- Maple syrup urine disease
- Classical galactosaemia
- Cystic fibrosis
- Congenital hypothyroidism.

Cystic Fibrosis is the latest addition in July 2011. There are plans to test for more conditions in the future.

Prevalence

Phenylketonuria is an inborn error of protein metabolism. The essential amino acid phenylalanine cannot be metabolised due to the absence of the liver enzyme phenylalanine hydroxylase. Normally, phenylalanine is needed for protein synthesis and is converted to tyrosine. Tyrosine is necessary for the synthesis of melanin, tyroxine and a number of neurotransmitters. In the absence of phenylalanine hydroxylase the individual with PKU is unable to convert phenylalanine to tyrosine which results in the inborn error of metabolism PKU. As a result, protein needs to be restricted in the diet.

Phenylketonuria is the most common amino acid disorder known and there is a very high incidence of the disorder in Ireland (see Table 1). It is an inherited autosomal recessive disorder (see Figure 1) ie. both parents are carriers of the mutation. With each pregnancy there is a 25% chance of the child inheriting the condition. Both girls and boys are equally affected.

PKU in newborns

Babies with PKU are the same at birth as any other newborn and so parents will be unaware if their child has PKU until a

Table 1: Incidence of phenylketonuria

Prevalence of PKU	Incidence per patient population
Worldwide	1: 12,000
Ireland	1: 4,500
Japan	1: 60,000
US	1: 14,000

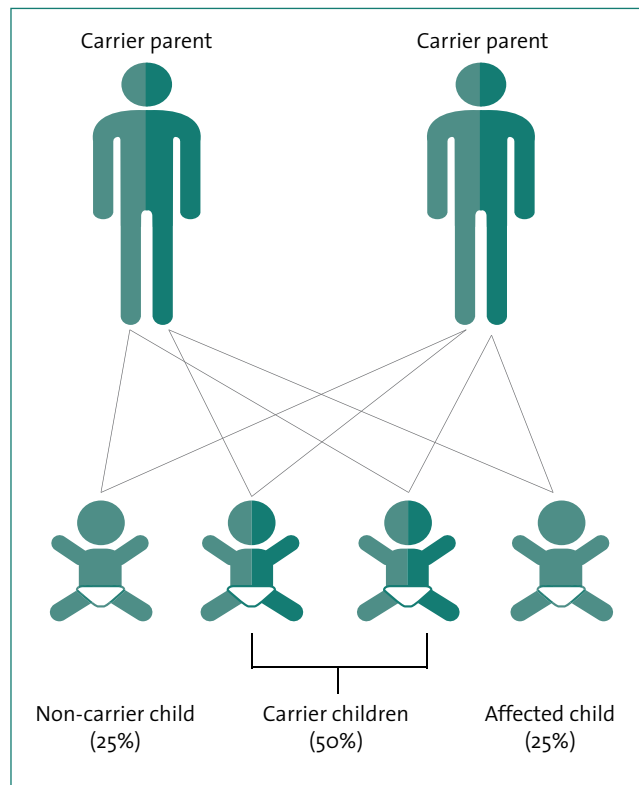


Figure 1. Autosomal recessive inheritance

positive result is reported by the National Newborn Screening Programme, which is based at the Children's University Hospital in Dublin.

Symptoms are due to the accumulation of phenylalanine which inhibits brain development and these will arise within the first few months of life if the condition is undiagnosed. In the untreated patient, the accumulation of phenylalanine results in intellectual disability, short attention span, poor short-term memory, problems with visual motor perception and motor coordination, seizures and behavioural problems. Undiagnosed cases would be an extremely rare occurrence in Ireland due to the National Newborn Screening Programme that is in place.

Screening for PKU

A newborn screening sample should be taken between 72 and 120 hours following birth and a repeat sample is done on day 10 of life to rule out PKU. Siblings of known cases generally have an

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elevated level of phenylalanine on the first sample if they have PKU.

Therapeutic management

Early diagnosis and prompt treatment with diet is needed to prevent damage to the developing brain. Dietary treatment is lifelong and its aims are to:

- Keep phenylalanine levels within the recommended range according to the treatment guidelines used by the National Centre
- Replace tyrosine and prevent deficiencies
- Provide adequate protein, energy, vitamins and minerals for growth and development.

Basic principle and components of dietary treatment

Dietary treatment is challenging work for the metabolic dietitian. The basic principle of the diet is to severely restrict the substance which is not metabolised; in this case phenylalanine. The missing end product, which in PKU is tyrosine, then has to be replaced. Normal growth is achieved by giving synthetically made protein devoid of phenylalanine and augmented with tyrosine. In addition, small amounts of natural protein are prescribed.

Careful dietetic supervision is essential to ensure an adequate intake of protein, calories, minerals, vitamins and trace elements. Monitoring of height and weight, regular blood tests to determine phenylalanine and tyrosine levels and nutritional status are all essential parts of the treatment.

High biological protein rich foods must be avoided as they contain an abundance of the toxic amino acid phenylalanine. However, children need a normal to high intake of other essential amino acids, as total protein needs remain similar to that of normal children. Protein requirements reduce as the child gets older and stabilise into adulthood. In order to achieve this diet, it is divided into three components:

- Synthetic protein
- Natural protein – commonly called protein exchanges
- Free foods.

Synthetic protein

In PKU, the synthetic protein is devoid of phenylalanine but contains the other 20 amino acids. Examples of these formulas are:

- *PKU Anamix Infant*: A complete infant formula this has the same nutritional composition as all standard infant formulae except it is devoid of phenylalanine. It is made up the same way ie. scoop of formula to 30mls or 1oz of water
- For older children there is a variety of drinks, pastes and gels
- *PKU gel and PKU Anamix Junior LQ for children*: These formulae are nutritionally complete
- *PKU express and PKU Lophlex*: Products for older children and adults, these formulae are nutritionally complete.

Synthetic protein formulae are expensive and can have a bitter aftertaste. Some children and adults have difficulty complying with their prescription. The amount of synthetic protein prescribed depends on weight. Synthetic protein should be divided into three or four drinks each day. These products are available in Ireland under the Long-Term Illness Scheme. PKU is the only metabolic disorder recognised under the Long-Term Illness Scheme. It allows patients to get drugs, medicines and medical and surgical appliances directly related to the treatment of PKU, free of charge. It does not depend on income or other circumstances and is separate from the medical card scheme and the GP visit card scheme. Without this being available to patients, dietary treatment would cost around €12,000 per annum. Dietary treatment is also free in

the UK but this is not the case internationally.

Natural protein (protein exchanges)

A small amount of phenylalanine is needed for normal growth. This is provided by a system of exchanges of natural protein each containing 1g of protein (1 exchange = 1g protein). Commonly used exchange foods include measured amounts of low biological based protein foods such as cereal, pasta, beans and peas.

Examples of 1g protein/1 exchange

- Two tablespoons of peas
- One tablespoon of baked beans
- Two tablespoons of chick peas

Most patients with phenylketonuria tolerate only a small number of exchanges (between four and eight per day). This allows for some flexibility but can be challenging to manage on a day-to-day basis. The aim of the treatment is to give sufficient phenylalanine for growth. This is achieved by keeping the blood phenylalanine levels as close to the normal physiological levels as possible. Patients are advised on the number of protein exchanges allowed based on frequent blood monitoring. It is important to note that aspartame must be avoided. This sweetener is often found in diet fizzy drinks.

Free foods

These contain only negligible amounts of protein. They are used to provide calories and add variety to the diet and fall into two categories:

- Naturally occurring foods such as fruit and vegetables (except peas, beans, sweetcorn and potatoes), sugars, jams, sweet drinks, fats and oils
- Specifically manufactured low protein (LP) products, eg. LP bread, rolls and flour, LP biscuits and crackers, LP Pasta, LP pizza bases, LP milk. These are all available on prescription.

Issues throughout the lifecycle

Children, as they get older, are encouraged to take responsibility for their diet. The teenage years can be a challenging time as they gain independence. Young women are advised that a pregnancy must be planned. Prior to conception, phenylalanine levels should be within the physiological range. High phenylalanine levels can have teratogenic effects on the foetus.

Illness

Catabolism associated with even mild illness/infection may cause the precursor phenylalanine to rise despite dietary compliance. In phenylketonuria this should not have any severe pathological effect in the short-term.

Patients with phenylketonuria should not be prescribed medications containing aspartame as it is a source of phenylalanine.

Points to remember

Should a patient with PKU be admitted or referred to your service, do not panic and keep in mind the following points:

- PKU is not a life-threatening disorder.
- Parents/patients manage at home every day so can continue to do so without your service
- For queries and advice call the National Centre for Inherited Metabolic Disorders at Tel: 01 8784317 and press 2 for the dietitian, or email: metabolic.dietitians@cuh.ie
- Visit our website www.metabolic.ie where you will find more information on PKU, the other metabolic disorders treated in the National Centre and many dietetic resources, which you are welcome to download and use.

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