NSPKU
The National Society for Phenylketonuria (United Kingdom) Ltd.

The Child with PKU

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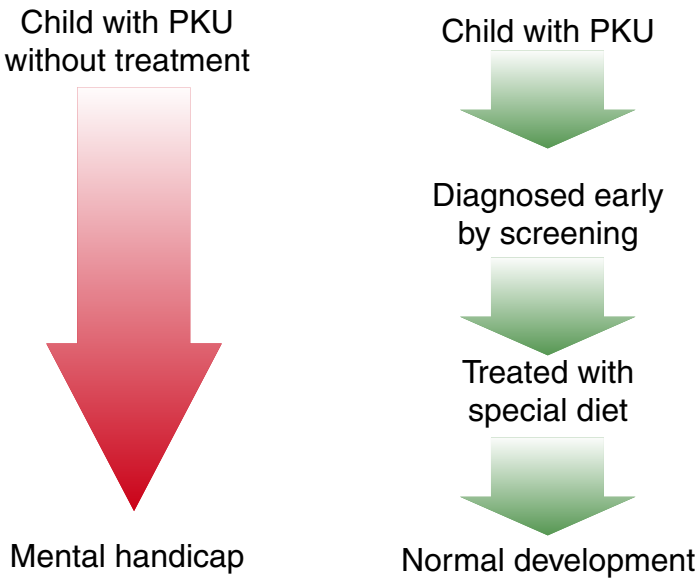
WHAT IS PKU?

Your child has a condition called phenylketonuria (PKU). This is a serious condition but, with treatment, your child will grow into a healthy adult. In this booklet, we explain what causes PKU and how it is treated.

Babies with PKU appear to be normal but their blood contains too much of a substance called phenylalanine. All babies in the UK have a test to see if there is too much phenylalanine in their blood. This is called a 'screening' test. If it is positive, a further blood test is done to confirm that the baby has PKU. Treatment is started as soon as possible, usually by the age of 3 weeks.

If the amount of phenylalanine in blood remains high for many months, it is harmful to the brain. In the past, before treatment was available, most children with PKU had severe mental handicap. This can be prevented now that we can treat affected children from a young age.

Phenylalanine is a natural part of most foods. PKU is treated with a special diet that is low in phenylalanine. This will bring the amount of phenylalanine in blood down to a safe level. If the diet is monitored carefully, your baby's brain will develop normally. Apart from the special diet, he or she will have a normal lifestyle.



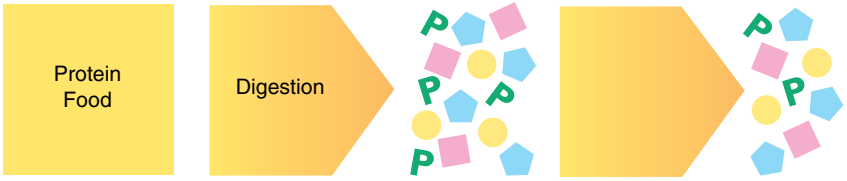
WHAT IS PHENYLALANINE?

Most foods contain a combination of 3 things:

- Proteins
- Fats
- Sugars (carbohydrates)

Different foods contain different amounts of protein. Meat, fish, eggs, milk and cheese are particularly high in protein. Proteins are formed from 'building blocks' called amino acids. There are 20 different amino acids and phenylalanine is one of them.

When proteins are eaten, they are digested in the gut. This involves breaking the links that join the amino acids together. The amino acids, including phenylalanine, are then absorbed into the bloodstream. From the blood, amino acids are taken up by various parts of the body for growth and repair.



containing amino acids

Amino acids used for growth and tissue repair including phenylananine (**P** in diagram)

Excess amino acids 'left over' following growth and tissue repair

WHY DO PEOPLE WITH PKU HAVE TOO MUCH PHENYLALANINE IN THEIR BLOOD?

People on a normal diet consume more amino acids than they need. The extra amino acids are broken down. The break-down takes several steps. Each of these steps is promoted by something called an enzyme. The first step in the break-down of phenylalanine is for it to be converted to another amino acid, called tyrosine. The enzyme needed for this step is called phenylalanine hydroxylase (PAH).

Phenylalanine metabolism in the non-PKU

Phenylalanine metabolism in the PKU

In patients with PKU, PAH is not working properly. This means that phenylalanine cannot be broken-down and its level in blood gets very high. On the other hand, tyrosine levels tend to be low, because it is normally made in the break-down of phenylalanine.

Tyrosine is used for building proteins. It is also used to make a number of chemicals, including dopamine and melanin. Dopamine has important functions in the brain. Melanin is a brown pigment and the colour of our skin, hair and eyes is affected by the amount of melanin present.

If children with PKU go for many months without treatment, it leads to brain damage. This is mainly because of the high phenylalanine levels in the blood and the brain. If children are not treated for years, they tend to have blond hair and blue eyes. This is because of the low levels of tyrosine and melanin.

THE TREATMENT OF PKU

PKU is treated with a diet that is very low in phenylalanine. All naturally occurring proteins contain phenylalanine so the diet can only contain very small amounts of protein. On the other hand, children need substantial amounts of protein to allow them to grow. To solve this problem, people with PKU use both

- a diet that is very low in natural protein
- a 'protein substitute' that contains tyrosine and all the other amino acids except phenylalanine.

People with PKU also need extra vitamins and minerals, such as calcium, because these tend to be low in their special diet. Many protein substitutes include the necessary vitamins and minerals.

THE PKU DIET IN BABIES

As soon as it has been confirmed that your baby has PKU, he or she will be started on a special baby milk. This will contain no phenylalanine but it will contain all the other amino acids (the protein substitute) and other things found in normal milk (sugars, fats, vitamins and minerals, such as calcium). The phenylalanine level in blood will fall to the acceptable range within a few days.

At that stage, some of your breast milk or ordinary baby milk will be added. This will provide a small amount of phenylalanine and prevent the blood phenylalanine levels from falling too low. Everyone needs some phenylalanine for growth, even people with PKU.

- If you are bottle feeding your baby, you will
  1. start each feed with a small, measured amount of ordinary baby milk
  2. then give as much as the baby wants of the special milk that contains no phenylalanine
- If you are breast feeding your baby, you will
  1. start most feeds with a measured amount of the special milk that contains no phenylalanine
  2. then breast feed on demand.

Giving the special milk first will make the baby less hungry and prevent the baby from taking too much breast milk.

HOW DO WE CHECK THE DIET IS WORKING?

It is important to keep your child's phenylalanine levels in a safe range, neither too high nor too low. The target range depends on his or her age. For babies, most centres aim to keep the blood phenylalanine level above 100-120 µmol/l and below 360-400 µmol/l. Every patient with PKU has levels outside the target range from time to time, for example during colds or other illnesses. Unless the phenylalanine level is too high or too low for a long period, it will not lead to any harm. The blood phenylalanine level is normally measured every week in babies with PKU. If the level is outside the target range, your dietitian will advise you how your child's diet needs to be changed.

The blood samples can be obtained from a heel-prick (or a finger-prick when your child is older). Samples are usually sent by post if you do not need to go to the hospital for another reason. Parents soon learn how take the samples, though many find the idea scary at first. The NSPKU has a leaflet to help with this.

THE PKU DIET IN OLDER CHILDREN

Babies with PKU can be weaned onto solid foods at the usual age, around 4-6 months. Foods that are very low in phenylalanine are started first. These include fruits, most vegetables and some baby foods. Your dietitian will give you detailed advice. At this stage, you should continue to give your baby some breast milk or some normal baby milk to provide the small amount of phenylalanine that is needed each day. Later, this will be replaced by foods containing phenylalanine, such as potatoes or cereals. You will need to weigh these foods to ensure that you give the right amount. Again, your dietitian will give you detailed instructions.

As your child takes more solids, he or she will take less of the special baby milk that contained the protein substitute – the mixture of all the amino acids except phenylalanine. Your child will continue to need a protein substitute. For this reason, a different form of protein substitute will be started at this stage.

Your child will have to avoid a number of foods, but special low-protein foods are made for people with PKU. These include special bread, biscuits, pasta etc. Your doctor will give you a prescription for these and your local chemist will be able to get them for you.

WHAT FOODS CAN BE EATEN?

NOT ALLOWED

Eggs

Meat

Fish

Nuts

RESTRICTED

Cereals

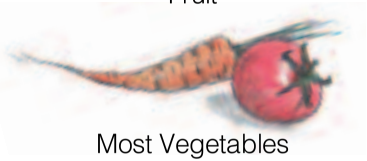
Chips/potatoes

Corn on the cob

Crisps

ALLOWED FREELY

Fruit



Most Vegetables

Honey/jam

Fruit Lollies

CAN THE PKU DIET EVER BE STOPPED?

Children must remain on a strict low phenylalanine diet at least until the age of 10 years. It used to be thought that the diet could safely be stopped at the age of 10-14 years. Now it is recommended that people with PKU should stay on their diet throughout life, though higher phenylalanine levels are allowed in older patients.

Despite these recommendations, many adults with PKU choose to stop dietary treatment. A few complain of lethargy, irritability or poor concentration when their blood phenylalanine levels are high but hardly any have developed serious problems. As yet, few of these people are more than 40 years old, so we do not know what may happen later. Brain scans show some changes in adults with high blood phenylalanine levels. Fortunately, these changes do not seem to cause problems.

Age	Recommended blood phenylalanine levels
Less than 4 years	120 to 360 µmol/l
4-10 years	120-480 µmol/l
More than 10 years	120-700 µmol/l
Pregnancy	100-250 µmol/l

Adults with PKU should attend a PKU clinic, even if they are on a 'normal' diet. This is because vitamin and mineral deficiencies are more common in adults with PKU. PKU clinics can look for these deficiencies and correct them, if necessary, before they cause problems. Attending a PKU clinic also allows adults to keep up to date with developments in treatment and research.

It is *extremely important* for women with PKU to be on a strict diet for pregnancy. See page 10.

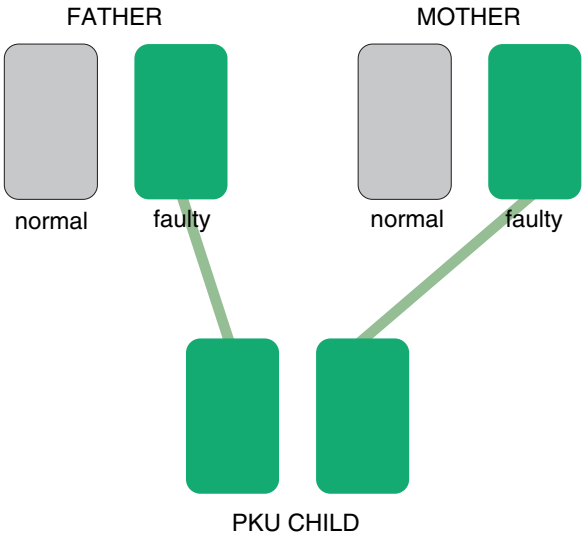
WHY DOES YOUR CHILD HAVE PKU?

Your child has inherited PKU from you and from your partner. This may come as a surprise because it is unlikely that either of you has PKU. In most families there are no relatives with PKU.

On page 3, we explained that phenylalanine is broken down by

phenylalanine hydroxylase (PAH). PAH is made using instructions that are called the PAH gene. Everyone has two copies of this gene in each cell of their body. One copy comes from their mother and one from their father. In people with PKU, such as your child, both copies of the PAH ***gene*** are faulty.

People with one faulty copy and one normal copy of the PAH gene are said to be 'carriers'. In the UK, approximately 1 person in 60 is a carrier for PKU. This is the situation in you and your partner. You do not have PKU because your normal copy of the PAH gene allows you to break down phenylalanine. Carriers can pass their faulty copy of the gene onto their children and this is how you have had a child with PKU.

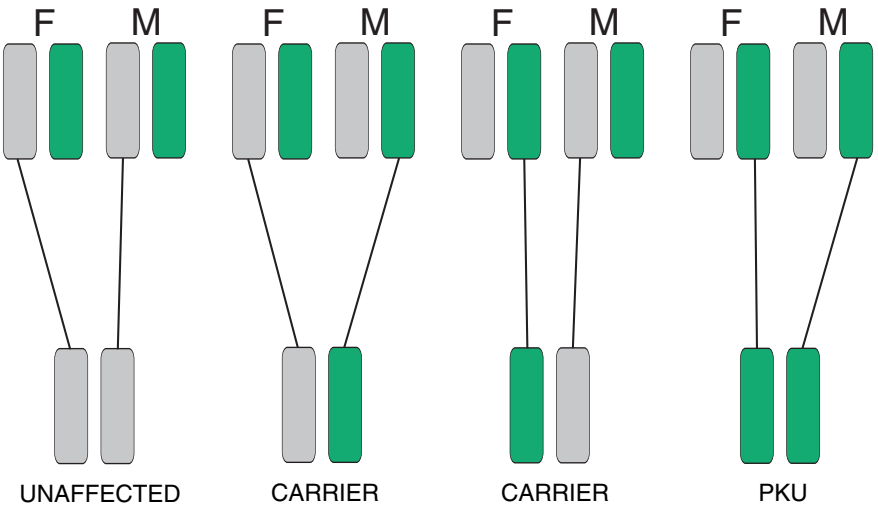


WILL ALL YOUR CHILDREN HAVE PKU?

No, you can have children who do not have PKU. You and your partner each have one normal copy of the PAH gene. If either of you passes on a normal copy, the child will not have PKU. The 4 possible combinations are shown below:

Only one of the 4 combinations would lead to a child with PKU. This means that each time you and your partner have a baby, there is a 1 in 4 chance that he or she will have PKU. There is a 2 in 4 chance of the child being a

carrier and a 1 in 4 chance of him or her inheriting both of the unaffected genes. The chances of having further children with PKU are not altered by having already had a child with PKU: you cannot expect three children without PKU before you have another affected child! Occasionally, parents who are carriers have three children in a row with PKU. There are also families where both parents are carriers but they remain unaware of this because none of their children have PKU.



IS PKU EQUALLY SEVERE IN EVERYONE?

No. People with PKU all have 2 faulty copies of the PAH gene. The faults are known as mutations and many different mutations are possible. Some mutations are more severe than others. Some mutations completely prevent the break-down of phenylalanine. Other mutations allow a little phenylalanine to be broken down at a slower rate than normal. To keep their phenylalanine levels in the target range, people with severe mutations have to stick to a stricter diet than people with mild mutations. Tests can be done to identify the mutations that have caused PKU in your child. These tests take several months; they are necessary if you want to avoid having further children with PKU.

CAN YOU AVOID HAVING FURTHER CHILDREN WITH PKU?

Many parents are prepared to risk having a second child with PKU, because it is a treatable condition. On the other hand, some parents would prefer not to have a second child with PKU.

If you know the mutations in your child with PKU, people can look for these mutations in future pregnancies. This can be done about 10 weeks into the pregnancy by taking a tiny piece of the baby's side of the placenta. It can also be done by amniocentesis later in the pregnancy. If the test shows that the baby is affected, it is possible to terminate the pregnancy.

CAN PEOPLE WITH PKU HAVE CHILDREN?

Yes, people with PKU can have children. Unless their partner happens to be a carrier, the children will not have PKU.

Unfortunately, if women with PKU have high phenylalanine levels when they are pregnant, this can damage their babies. If the mother is not on diet during pregnancy, the baby will almost certainly have mental handicap. The baby may also have malformations, for example affecting the heart. To avoid these problems, women who want a baby have to go onto a very strict diet. Frequent blood tests and careful supervision are essential. If the phenylalanine levels are good throughout pregnancy, a woman with PKU can expect a completely healthy baby. We strongly recommend that women with PKU keep their blood phenylalanine levels in the target range for a little while before they start trying to get pregnant. If an unplanned pregnancy should occur, advice should be sought *immediately*.

Men with PKU do not have to be on a special diet to father a child.

THE HISTORY OF PKU

Dr Folling was the first person to describe PKU in 1934. He worked in Norway and he was contacted by a mother who had two children with mental handicap. The mother had noticed that the children had a peculiar smell. He found a chemical in the urine and he worked out that it was a 'phenylketone'. Because this chemical was present in the urine, the condition was called phenylketonuria.

Dr Bickel was the first person to treat a patient with a low protein diet. This

was in 1956 at Birmingham Children's Hospital in England. Unfortunately, the patient was already handicapped before the diet was started. In those days, the diet was extremely difficult and the patient did not manage to stick to the diet for very long.

At first, a urine test was needed to make the diagnosis. Unless there was an affected brother or sister, the test was only done after the patient started to have problems. Dr Guthrie from the USA worked out how to test blood that had been collected on blotting paper. This allowed newborn babies to have a screening test. The screening test was first used in the UK in 1965 but many parts of the country only started using the test in 1969.

In 1992, Dr Woo found the gene for phenylalanine hydroxylase. This is the gene that is faulty in PKU. He was working in Houston, Texas, in the USA.

NSPKU

The National Society for Phenylketonuria is a charity run by people with PKU and their parents. Its main aim is to support families with PKU. It produces leaflets about various aspects of PKU. Each year it organises a conference for families with PKU. For further information contact the Society Helpline on 020 8364 3010 or visit our website **www.nspku.org**.

ABBREVIATIONS

PKU	Phenylketonuria
PAH	Phenylalanine hydroxylase
µmol/l	Micromoles per litre, a measurement of the amount of a substance in blood (or another liquid)

GLOSSARY

Amino acids	The 'building blocks' from which protein is made.
Enzyme	A special protein that helps a chemical reaction to take place. The enzyme that helps to break down phenylalanine is called phenylalanine hydroxylase.
Gene	The instructions for something about us that is inherited from our parents. The PAH gene is a set of instructions for making phenylalanine hydroxylase. People with PKU have faults (mutations) in this gene.
Mutation	A fault in a gene
Malformation	A structure in a baby that is faulty, for example, a hole between the two pumping chambers in the heart
Phenylalanine	One of the amino acids from which protein is made. It cannot be broken down in people with PKU
Phenylalanine hydroxylase	The enzyme that allows the body to break down phenylalanine
Phenylketones	Chemicals formed from phenylalanine and found in the urine of people with PKU
Protein	An important part of our food. Proteins have many functions in the body, including acting as enzymes.

Produced by the National Society for Phenylketonuria
and its Medical Advisory Panel.

N S P K U

The National Society for Phenylketonuria (United Kingdom) Ltd.

The Society is a registered charity.
It offers support to PKUs and their families by producing various publications including a quarterly newsletter, organising formal and informal meetings and conferences.

Further information and details can be obtained by contacting:
The NSPKU Helpline on: 020 8364 3010
or writing to:
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