



Genetic Fact Sheets for Parents

Amino Acid Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – [http:// www.newbornscreening.info](http://www.newbornscreening.info)

Disorder name: Phenylketonuria
Acronym: PKU

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This fact sheet contains general information about PKU. Every child is different and some of these facts may not apply to your child specifically. Certain treatments may be advised for some children but not others. All children with PKU should be followed by a metabolic doctor in addition to their primary care provider.

If your newborn has had a 'presumptive positive screen for PKU' as a result of newborn screening, it does not yet mean that he or she has PKU. There are other tests that need to be done to confirm whether your baby actually has PKU. Some babies are found not to have PKU and do not need treatment. Others are found to have a milder condition called "hyperphenylalaninemia" - also called 'hyperphe' or 'non-PKU HPA'. Many children with non-PKU HPA do not need treatment.

There is also another type of non-PKU HPA that is treated with a medication

called BH4 (tetrahydrobiopterin). This condition is rare (less than 2% of cases). Blood and urine tests can be done to determine whether your child has this type of non-PKU hyperphe.

This fact sheet contains information about classic PKU only. Therefore, the details below are relevant only to babies who have been confirmed to have classic PKU. It does not contain information on non-PKU HPA or other variants.

What is PKU?

PKU stands for “phenylketonuria.” It is one type of [amino acid disorder](#). People with PKU have problems breaking down an amino acid called phenylalanine from the food they eat.

Amino Acid Disorders:

Amino acid disorders (AAs) are a group of rare inherited conditions. They are caused by enzymes that do not work properly.

Protein is made up of smaller building blocks called amino acids. A number of different enzymes are needed to process these amino acids for use by the body. Because of missing or non-working enzymes, people with amino acid disorders cannot process certain amino acids. These amino acids, along with other toxic substances, then build up in the body and cause problems.

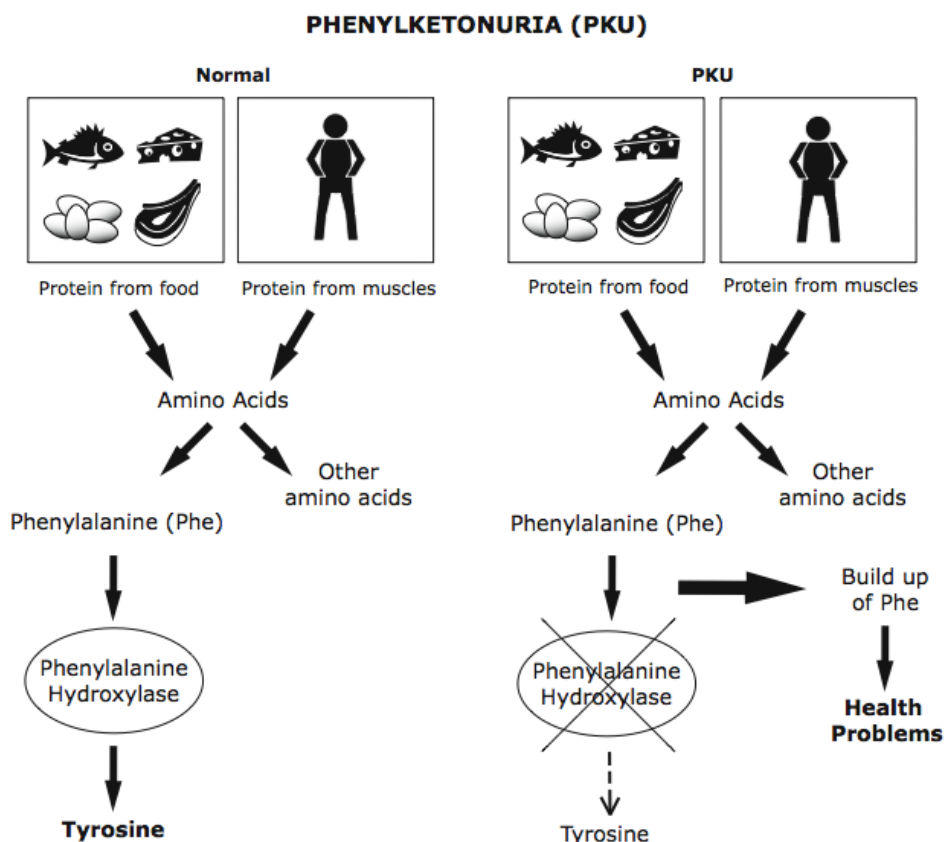
The symptoms and treatment vary between different amino acid disorders. They can also vary from person to person with the same amino acid disorder. See the fact sheets for each specific amino acid disorder.

Amino acid disorders are inherited in an autosomal recessive manner and affect both males and females.

What causes PKU?

In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them.

PKU occurs when an enzyme, called “phenylalanine hydroxylase” (PAH), is either missing or not working properly. The job of this enzyme is to chemically change the amino acid phenylalanine (Phe – pronounced ‘fee’) into other substances. When a child with PKU eats food containing Phe, it builds up in the blood and causes problems. Phe is found in almost every food, except pure fat and sugar.



If PKU is not treated, what problems occur?

Babies with PKU seem perfectly normal at birth. The first symptoms are usually seen around 6 months of age. Untreated infants may be late in learning to sit, crawl and stand. They may pay less attention to things around them. Without treatment, a child with PKU will have intellectual disabilities.

Some of the effects of untreated PKU include:

- intellectual disabilities
- behavior problems
- hyperactivity
- restlessness or irritability
- seizures
- a skin condition called eczema
- a “musty” or “mousy” body odor
- fair hair and skin

What is the treatment for PKU?

Your baby's primary doctor will work with a metabolic doctor and a dietician experienced with PKU to care for your child.

Prompt treatment is needed to prevent intellectual disabilities. Newborns need to drink a special medical formula. It is still possible to breastfeed your baby as long as you get help from your dietitian. Babies who are breastfed usually need the medical formula as well.

Most children need to eat a special diet made up of very low-protein foods, special medical foods, and the special formula. You must start the low-Phe diet as soon as you know your child has PKU. Your dietitian will create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. The diet should be continued throughout life.

The following are treatments often advised for children with PKU:

1. Medical formula

Even though they need less Phe, children with PKU still need a certain amount of protein. The medical formula gives babies and children with PKU the nutrients and protein they need while helping keep their Phe levels within a safe range.

Your metabolic doctor and dietitian will tell you what type of formula is best and how much to use. Some states offer help with payment and some require private insurance coverage for the formula and other special medical foods.

2. Low-Phe food plan

The low-Phe food plan is made up of foods that are very low in Phe which is found in protein. This means your child must avoid or strictly limit foods that are high in protein including the following foods:

- milk and all dairy products including cheese, yogurt, ice cream
- regular formula
- meat and poultry
- fish
- eggs
- nuts and peanut butter
- dried beans
- regular flour

It is very important that your child avoid the sugar substitute aspartame (sold under the brand names "Equal", Nutrasweet "Sweetmate", "Canderl"). Aspartame contains high amounts of Phe. It can quickly raise the blood levels of Phe in people with PKU. Your child must not have any diet foods or drinks that

contain aspartame. Some medicines and vitamins also contain aspartame. If you're not sure, ask your pharmacist, metabolic doctor, or dietician.

Many vegetables and fruits have only small amounts of Phe and can be eaten in carefully measured amounts. In addition, there are other medical foods such as low-Phe flours, baking mixes, breads, and pastas that are made especially for people with PKU.

Your child's food plan will depend on many things such as his or her age, weight, general health, and blood test results. Your dietician will fine-tune your child's diet over time.

Your child should follow this diet throughout life. Adults who do not stay on the diet and have high levels of Phe in their blood may notice some of the following:

- trouble paying attention
- problems making good decisions
- slow thinking
- irritability
- eczema
- bone loss (osteopenia)
- tremors

Women need to be on the low-Phe diet before becoming pregnant. They need to stay on the diet throughout pregnancy. This will lessen the chance for serious health and learning problems in their babies.

3. Tracking Phe levels

Babies and young children with PKU need to have regular blood tests to measure their Phe levels. If there is too much or too little Phe in the blood, the diet and formula may need to be adjusted.

4. Enzyme cofactors

Cofactors are proteins that help an enzyme function. BH4 (tetrahydrobiopterin) is a substance made by the body. Kuvan® (sapropterin dihydrochloride) is a synthetic form of this substance. Both work to help the PAH enzyme change Phe into Tyr.

Some children with PKU will benefit from taking enzyme cofactors in pill form. This treatment is helpful in reducing blood Phe levels in some children with PKU. About 10% of children with classic PKU respond to enzyme cofactors. Most children with mild PKU are helped by enzyme cofactors.

Your doctor can do blood tests to determine whether your child responds to enzyme cofactors. Do not take enzyme cofactors unless advised by your metabolic doctor.

5. Pregnancy in women with PKU (“Maternal PKU”)

Women with PKU who are not on the low-Phe diet when they become pregnant have a high chance of having babies with birth defects and intellectual disabilities.

Women who are not on the diet usually have high levels of Phe in their blood. The extra Phe gets to the fetus and causes problems with brain and body growth. Babies of untreated mothers may have the following:

- small brains
- intellectual disabilities
- birth defects of the heart
- low birth weight

This condition is called “maternal PKU syndrome.”

Women with PKU who want to have children need to have very low blood Phe levels before they get pregnant. During pregnancy, they need to:

- stay on the low-Phe diet
- visit their PKU clinic on a regular basis
- have their blood Phe levels checked often

What happens when PKU is treated?

Children with PKU who start treatment soon after birth and keep their Phe levels within the suggested range usually have normal growth and intelligence. Some children, even when treated, have problems with schoolwork and may need extra help.

If treatment is not started until several weeks after birth, delays or learning problems may occur. The level of delay varies from child to child.

Children who start treatment after 6 months of age often have intellectual disabilities. Treatment is still important, even if started late, because it can help control behavior and mood problems and can prevent further damage to the brain.

What causes the PAH enzyme to be absent or not working correctly?

Genes tell the body to make certain enzymes. THE PAH gene instructs the body how to make the PAH enzyme. People with PKU have changes in both copies of their PAH genes which cause them to not work correctly. Because of the changes, also called variants, in the PAH genes, the PAH enzyme either does not work properly or is not made at all.

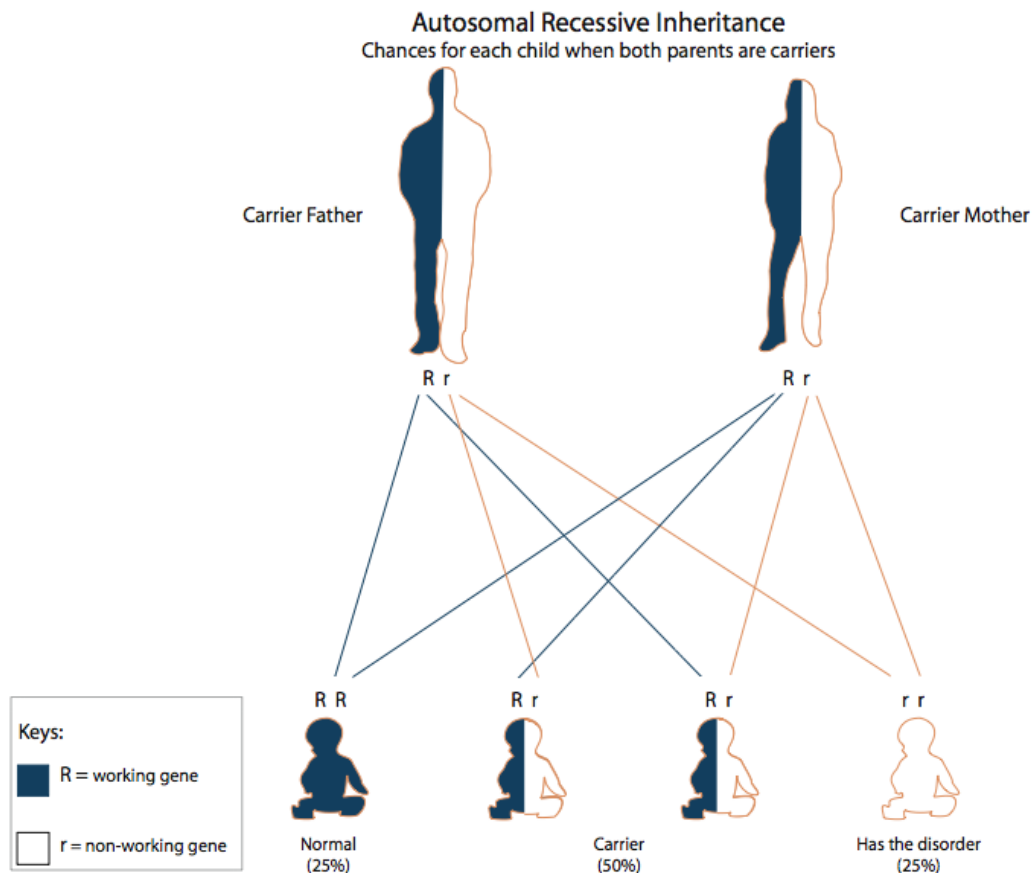
How is PKU inherited?

PKU is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies of the PAH gene that makes the PAH enzyme. In children with PKU, neither of these genes works correctly. These children inherit one non-working PAH gene from each parent.

Parents of children with PKU rarely have the condition themselves. Instead, each parent has a single non-working PAH gene. They are called carriers. Carriers do not have PKU because their other PAH gene is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have PKU. There is a 50% chance for the child to be a carrier, just like the parents. And, there is a 25% chance for the child to have two working genes.



Genetic counseling is available to families who have children with PKU. Genetic counselors can answer your questions about how PKU is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

Genetic testing for PKU is available. Genetic testing, also called DNA testing, looks for changes (variants) in the PAH genes that causes PKU.

DNA testing is not necessary to diagnose your child. It is sometimes helpful to know the gene changes in a child with PKU because it may help the doctors and dietician develop the best treatment plan. It is sometimes of help in determining which children will respond to biotin supplements. It can also be helpful for carrier or prenatal testing, discussed below.

What other testing is available?

PKU is confirmed by measuring the amount of Phe and Tyr in a blood sample. Talk to your doctor or your genetic counselor if you have questions about testing for PKU.

Can you test during a future pregnancy?

If both gene changes (variants) have been found in your child with PKU, DNA testing can be done during future pregnancies. The sample needed for this test is obtained by either CVS or amniocentesis.

Parents may choose to have testing during pregnancy or wait until birth to have the baby tested. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children would have PKU. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have PKU or be carriers?

Having PKU

If they are healthy and developing normally, older brothers and sisters of a baby with PKU are unlikely to have PKU. Talk to your doctor or genetic counselor if you have questions about your other children.

PKU carriers

Brothers and sisters who do not have PKU still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done in people over 18 years of age.

If you are a parent of a child with PKU, your brothers and sisters have a 50% chance to be a carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with PKU.

All states offer newborn screening for PKU. However, when both parents are carriers, newborn screening results are not sufficient to rule out the condition in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening. It is very important that this testing be done immediately – ideally at 24 hours of age.

Can other family members be tested?

Diagnostic testing

If there is concern about whether they have the condition, your other children can be tested to see if they also have PKU. Talk to your doctor or genetic counselor if you have questions about testing for PKU.

Carrier testing

If both gene changes in the PAH gene have been found in your child, other family members can have DNA testing to see if they are carriers. If DNA testing is not helpful, other methods of carrier testing may be available. If you have questions about carrier testing, ask your genetic counselor or metabolic doctor.

How many people have PKU?

About one in every 10,000 Caucasian babies in the United States is born with PKU.

Does PKU happen more frequently in a certain ethnic group?

PKU happens in people of all ethnic groups around the world. It happens more often in people whose families come from Ireland and other parts of Northern Europe. It is also more common in people from Turkey and those who are Native Americans. PKU is less common in people of African, Japanese, or Ashkenazi Jewish backgrounds.

About 1 in every 50 Caucasians is a PKU carrier.

Does PKU go by any other names?

PKU is sometimes also called:

- hyperphenylalaninemia – classic type
- phenylalanine hydroxylase deficiency
- PAH deficiency

Some variants of hyperphenylalaninemia not discussed in this fact sheet are:

- hyperphenylalanemia – mild type (non PKU-HPA)
- bipterin deficiency
- dihydropteridine reductase (DHPR) deficiency
- Guanosine triphosphate cyclohydrolase (GTPCH) deficiency
- 6-pyruvoyl tetrahydrobiopterin synthase (PTPS) deficiency
- Pterin-4 acarbinolamine dehydratase (PCD) deficiency

Where can I find more information?

National PKU Alliance

<http://www.npkua.org/>

Metabolic Support UK

<https://www.metabolicsupportuk.org>

Baby's First Test
<http://www.babysfirsttest.org>

MedlinePlus
<https://medlineplus.gov/genetics/condition/phenylketonuria/>

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