CONDITION

Phenylketonuria

Phenylketonuria is an inherited condition that prevents the body from properly processing phenylalanine from food.

WHAT IT IS
Inherited inability to process the amino acid phenylalanine

BODY SYSTEM
Brain and nervous system, metabolism

MAIN SYMPTOMS
Developmental delay, learning problems, seizures, behavioural changes

WHAT CAUSES IT
Inherited changes affecting phenylalanine breakdown

HOW IT IS DIAGNOSED
Newborn screening, blood amino acids, and genetic testing

MAIN TREATMENT
Lifelong diet management, medical foods, and medicines

CAN IT BE CURED?
No - the inherited enzyme deficiency remains lifelong

IS IT AN EMERGENCY?
Sometimes, breathing trouble after medicine signals severe allergy

LONG-TERM OUTLOOK
Usually healthy lives with early, sustained treatment

Overview

Phenylketonuria, usually called PKU, is an inherited condition that affects how the body handles phenylalanine. Phenylalanine is an amino acid, one of the building blocks of protein. It is found in many everyday foods.

Most people with PKU have too little working phenylalanine hydroxylase. This enzyme normally changes phenylalanine into another amino acid called tyrosine. Without enough enzyme activity, phenylalanine builds up in the blood and brain.

High phenylalanine levels can interfere with brain development and function. Babies with PKU usually appear healthy at birth, so newborn screening is important. Treatment started soon after birth can prevent most serious effects.

PKU remains lifelong, but it can usually be managed. Treatment aims to keep phenylalanine within a safe target range while providing enough protein, energy, vitamins, and minerals for normal growth and health.

Symptoms

A baby diagnosed and treated through newborn screening may have no noticeable symptoms. Symptoms are more likely when PKU is untreated, diagnosed late, or not adequately controlled.

Possible effects include:

Older children and adults whose phenylalanine levels are high may notice problems with concentration, processing information, mood, anxiety, or mental tiredness. These symptoms can have many causes and do not confirm PKU.

Adults treated from infancy usually do not develop the severe intellectual disability associated with untreated PKU. However, some still experience subtle difficulties with attention, organisation, or emotional well-being, especially during periods of higher phenylalanine levels.

- Delayed development or intellectual disability
- Difficulties with attention, planning, memory, or learning
- Behavioural or emotional problems
- Seizures
- A smaller-than-expected head size
- Eczema, an itchy inflammatory skin condition
- A musty or unusual smell of the skin, breath, or urine
- Lighter skin and hair than other family members

Causes and risk factors

PKU is usually caused by changes in the PAH gene. This gene provides instructions for making phenylalanine hydroxylase.

The condition follows an autosomal recessive inheritance pattern. This means a child usually inherits one altered copy of the gene from each parent. The parents are generally healthy carriers and may not know they carry the change.

When both parents are carriers, each pregnancy has:

These chances apply separately to each pregnancy. They are not changed by the outcome of an earlier pregnancy.

Different gene changes leave different amounts of enzyme activity. This is one reason phenylalanine tolerance and treatment needs differ between people. PKU is not caused by something a parent ate or did during pregnancy.

Rarely, high phenylalanine has another cause, such as a problem producing or recycling tetrahydrobiopterin, also called BH4. BH4 helps several enzymes work. Tests after an abnormal newborn screen help distinguish these conditions.

- A 1 in 4 chance that the child will have PKU
- A 1 in 2 chance that the child will be a healthy carrier
- A 1 in 4 chance that the child will inherit neither altered copy

Diagnosis

In many countries, PKU is first detected through newborn blood spot screening. A small blood sample is usually collected from the baby's heel during the first days of life.

A screening result does not by itself confirm PKU. If phenylalanine is high, follow-up testing is arranged promptly. This generally includes a blood amino acid test to measure phenylalanine and related substances.

Genetic testing may identify changes in the PAH gene. It can help confirm the cause, estimate whether certain medicines might work, and provide information for family testing. Tests for BH4-related conditions may also be needed.

Someone born before screening became routine, or in a place without screening, may be tested later because of developmental, learning, neurological, or behavioural concerns.

After diagnosis, regular blood tests measure phenylalanine. The recommended target range can change with age, pregnancy, treatment, and local guidance. The metabolic team will explain the appropriate range and how often testing is needed.

Treatment and management

PKU treatment is usually coordinated by a specialist metabolic team. It is personalised because people differ in how much natural protein they can process.

Food and medical nutrition

The main treatment is a phenylalanine-controlled eating plan. High-protein foods usually need to be limited or measured. These may include meat, fish, eggs, dairy products, nuts, beans, and ordinary flour-based foods.

Phenylalanine cannot be removed completely because the body needs a small amount. Cutting out protein without specialist support can cause poor growth and nutrient deficiencies.

Most people use a prescribed protein substitute or medical formula. It supplies protein without phenylalanine, along with nutrients that may otherwise be difficult to obtain. Special low-protein foods can provide energy and make meals more practical.

Aspartame, an artificial sweetener, contains phenylalanine and generally needs to be avoided. Packaged foods containing it usually carry a phenylalanine warning.

Babies with PKU may receive measured breast milk or standard infant formula alongside a phenylalanine-free formula. Frequent blood testing guides the balance.

Medicines

Some people have gene changes that leave part of the enzyme working. They may respond to a medicine that helps the remaining enzyme process phenylalanine. A response is confirmed through testing rather than assumed.

Injectable enzyme replacement may be an option for some adults whose phenylalanine remains high despite other management. It can cause serious allergic reactions, so it requires specific safety precautions and monitoring.

Other treatments may be available depending on age, treatment response, and approval in the country where you live. Medicines support dietary management for many people rather than replacing all monitoring.

Ongoing monitoring

Routine care may include:

Pregnancy requires particularly close monitoring. Phenylalanine should be controlled before conception and throughout pregnancy because high levels can harm the developing baby.

- Home or clinic blood samples for phenylalanine
- Checks of growth, weight, and nutritional intake
- Blood tests for iron, vitamin B12, vitamin D, and other nutrients
- Reviews of learning, attention, mood, or mental health
- Bone health assessment when clinically appropriate

Complications

The main complication of untreated PKU is lasting injury to the developing brain. This can lead to severe intellectual disability, seizures, and major behavioural difficulties. Early treatment greatly reduces this risk.

Even in treated people, persistently high phenylalanine may affect attention, planning, reaction speed, mood, or school and work performance. Effects are not the same for everyone.

A very restrictive diet that is not nutritionally balanced can cause low levels of protein, iron, vitamin B12, vitamin D, calcium, or other nutrients. This is why medical formula and dietitian follow-up are important.

PKU and pregnancy

A person with PKU can have a healthy pregnancy, but high phenylalanine during pregnancy can cross the placenta. The developing baby may then have poor growth, a small head, heart differences, or intellectual disability. This can happen even if the baby does not inherit PKU.

Planning should ideally begin before pregnancy. Early contact with the metabolic and pregnancy teams is important if pregnancy occurs unexpectedly.

PKU in a biological father does not expose the developing baby to high phenylalanine through the bloodstream. However, the child may inherit an altered gene.

Prevention

PKU itself cannot usually be prevented because it is inherited.

Newborn screening does not prevent the condition, but it allows treatment to begin before high phenylalanine causes major harm. Consistent treatment can prevent many complications.

If PKU or a related gene change is present in your family, genetic counselling can explain carrier testing, inheritance, and reproductive options. These choices are personal, and counselling is intended to provide information rather than direct a decision.

For someone with PKU who may become pregnant, controlling phenylalanine before conception and during pregnancy helps protect the developing baby.

Living with it and what to expect

PKU management continues through childhood, adulthood, and older age. Most people diagnosed through newborn screening can attend school, work, form relationships, travel, and

raise families.

Daily life often involves planning meals, taking medical formula, checking labels, avoiding aspartame, and sending blood samples. The amount of natural protein tolerated may change with growth, illness, pregnancy, or treatment.

Adolescence and early adulthood can be challenging because eating becomes more independent. Preparing for the move from children's services to adult care can help prevent gaps in treatment.

Some adults were previously advised that they could stop dietary treatment. Current management generally supports lifelong phenylalanine control because the adult brain can also be affected. Returning to treatment may improve concentration, mood, or mental clarity for some people, although the degree of improvement cannot be predicted.

Illness can temporarily raise phenylalanine as the body breaks down its own protein. A metabolic team can provide an illness plan covering fluids, energy intake, formula, medicines, and blood testing.

Long-term research on ageing with PKU is still developing. Regular follow-up remains useful even when you feel well, because blood levels and nutritional shortages may not cause obvious early symptoms.

When to get medical help

Arrange routine follow-up if blood phenylalanine results are repeatedly outside your target, you are struggling to take medical formula, or the eating plan has become difficult to maintain. New concentration, mood, learning, or nutritional concerns also deserve review.

Contact the metabolic team promptly if you cannot keep down food or formula, have a prolonged illness, or are likely to run out of medical supplies.

Seek early specialist advice if you are planning a pregnancy, think you may be pregnant, or have a positive pregnancy test. This is time-sensitive but is not usually an emergency.

Call emergency services for a seizure lasting several minutes, repeated seizures without recovery, severe breathing difficulty, collapse, or unresponsiveness.

A serious allergic reaction can occur with some injectable PKU treatments. Use the emergency plan provided with the medicine and seek emergency care for breathing trouble, throat or tongue swelling, faintness, or widespread hives accompanied by other symptoms.

Common questions

Can PKU go away?

No. The inherited change affecting phenylalanine processing remains lifelong. Treatment can keep phenylalanine controlled and prevent many complications, but it does not remove the underlying genetic cause.

What foods should someone with PKU avoid?

Many high-protein foods need to be limited or measured. Aspartame generally needs to be avoided. The exact allowance is individual, so food changes should be based on a metabolic dietitian's plan rather than a standard online food list.

Is PKU a food allergy?

No. An allergy is an immune reaction to a substance. In PKU, the body cannot process phenylalanine normally. Eating too much phenylalanine raises its level rather than causing an immediate allergic reaction.

Can someone with PKU have children?

Yes. People with PKU can become parents. A person who may become pregnant needs careful phenylalanine control before and during pregnancy to protect the developing baby. Genetic counselling can explain the chance of a child inheriting PKU.

Can a baby with PKU be breastfed?

Often, yes. Breast milk contains phenylalanine, so the amount usually needs to be balanced with phenylalanine-free formula and guided by frequent blood tests. A specialist team can support feeding while making sure the baby receives enough nutrition.

What happens if an adult stops the PKU diet?

Phenylalanine usually rises. Some adults develop problems with concentration, planning, mood, anxiety, or mental tiredness, while others notice little at first. Regular monitoring is important because high levels may not cause immediate symptoms.

Sources

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