CONDITION

Pyruvate kinase deficiency

Pyruvate kinase deficiency is an inherited condition that causes red blood cells to break down too early.

WHAT IT IS
Inherited red blood cell enzyme condition causing lifelong haemolytic anaemia

BODY SYSTEM
Blood and circulation

MAIN SYMPTOMS
Fatigue, pale skin, jaundice, shortness of breath

WHAT CAUSES IT
Inherited PKLR gene changes

HOW IT IS DIAGNOSED
Pyruvate kinase enzyme testing and PKLR genetic testing

MAIN TREATMENT
Supportive care, transfusions, medicines, or selected surgery

CAN IT BE CURED?
Sometimes - stem cell transplant can cure it

IS IT AN EMERGENCY?
Sometimes - sudden severe anaemia or post-splenectomy fever

LONG-TERM OUTLOOK
Lifelong condition ranging from mild to medically complex

Overview

Pyruvate kinase deficiency is an inherited condition affecting red blood cells. It is present from birth, although mild cases may not be recognised until later in life.

Red blood cells need an enzyme called pyruvate kinase to make energy. An enzyme is a protein that helps a chemical process happen. Without enough working pyruvate kinase, red blood cells become fragile and break down sooner than normal. This is called haemolysis .

The bone marrow tries to replace the lost cells, but it may not keep up. This causes haemolytic anaemia , meaning there are too few healthy red blood cells to carry oxygen around the body. The breakdown of red blood cells also releases bilirubin, a yellow pigment that can cause jaundice and gallstones.

The effects differ widely. Some people have mild anaemia and few symptoms. Others need regular transfusions or develop complications such as iron overload. A person's haemoglobin level does not always show the full effect on their health.

Symptoms

Symptoms can begin during the newborn period, childhood, or adulthood. They may remain fairly steady or become more noticeable during infections, pregnancy, or other physical stress.

Common symptoms include:

Newborn babies may develop significant jaundice or anaemia. Some need treatment soon after birth. In rare, severe cases, anaemia begins before birth.

Children may grow normally, but severe or poorly controlled anaemia can affect energy, school attendance, growth, or puberty. Adults may have symptoms even when their anaemia has been present for years because the body can compensate only partly.

- Tiredness, low stamina, or difficulty concentrating
- Pale skin or pale tissue inside the mouth
- Yellow skin or eyes, known as jaundice
- Shortness of breath, especially during activity
- A fast or pounding heartbeat
- Darker urine during increased red blood cell breakdown
- An enlarged spleen, which may cause fullness under the left ribs
- Gallstones, which can cause pain in the upper right abdomen

Causes and risk factors

Pyruvate kinase deficiency is caused by changes in the PKLR gene. This gene gives the body instructions for making pyruvate kinase in red blood cells.

The condition is usually inherited in an autosomal recessive pattern. This means a person generally has a non-working gene copy from each biological parent. The parents are usually carriers and do not have symptoms.

When both parents are carriers, each pregnancy has:

These chances apply separately to every pregnancy. Different PKLR gene changes can affect

how much enzyme activity remains, but genetic results cannot always predict exactly how someone will be affected.

Pyruvate kinase deficiency is not caused by diet, infection, or anything the parents did during pregnancy.

- A 1 in 4 chance that the child will have the condition
- A 1 in 2 chance that the child will be a carrier
- A 1 in 4 chance that the child will inherit neither gene change

Diagnosis

Diagnosis begins with blood tests. A complete blood count can show anaemia, while a reticulocyte count measures young red blood cells. The reticulocyte count is often raised because the bone marrow is trying to replace cells that have broken down.

Other tests may show signs of haemolysis, including increased bilirubin and lactate dehydrogenase, with reduced haptoglobin. A blood film allows the cells to be examined under a microscope. These findings suggest haemolysis but do not prove pyruvate kinase deficiency.

Confirmation usually involves:

Recent transfusions can make enzyme results appear more normal because donor red blood cells contain working pyruvate kinase. Large numbers of young red blood cells may also affect the result. Testing may therefore need careful timing or repetition. Genetic testing can help confirm the diagnosis when enzyme results are unclear.

Testing may also rule out other inherited red blood cell conditions, immune causes of haemolysis, and enzyme deficiencies with similar features.

Once the diagnosis is established, further tests assess iron levels, liver health, gallstones, bone health, and other possible complications. Family members may be offered testing when appropriate.

- Measuring pyruvate kinase activity in red blood cells
- Genetic testing for disease-causing changes in the PKLR gene

Treatment and management

Treatment is based on symptoms, complications, age, and the effect of anaemia on daily life. Not everyone needs the same level of treatment.

Blood transfusions provide healthy red blood cells. Some people need them only during illness, surgery, or pregnancy. Others need regular transfusions. Decisions are usually based on symptoms and overall health rather than a single haemoglobin result.

Folic acid may be recommended because the bone marrow uses it while making new red blood cells. Iron supplements should not be started simply because anaemia is present. People with pyruvate kinase deficiency can build up too much iron, including those who receive few or no transfusions.

Iron overload is monitored with blood tests and, when needed, MRI scans of the liver or heart. Medicines called iron chelators can remove excess iron from the body.

Removing the spleen, called splenectomy , may improve anaemia and reduce transfusion needs in selected people. It does not cure the condition, and haemolysis continues. Splenectomy also increases the lifelong risk of serious infection and blood clots. Vaccination, infection precautions, and a clear plan for managing fever are important after this surgery.

Mitapivat is a medicine that activates pyruvate kinase and may improve anaemia or reduce transfusion needs in some adults. Whether it is suitable depends partly on the person's PKLR gene changes and local approval. It requires monitoring and should not be stopped suddenly without medical guidance.

A stem cell transplant can replace the blood-forming system and potentially cure pyruvate kinase deficiency. However, transplantation carries significant short- and long-term risks. It is generally considered only for selected people with severe complications. Gene therapy remains under investigation.

Gallbladder surgery may be needed for painful or complicated gallstones. Pregnancy may require closer blood monitoring and coordinated specialist care.

Complications

Iron overload is one of the most important long-term complications. It can result from transfusions, but the body may also absorb too much iron from food because of ongoing anaemia. Untreated iron overload can damage the liver, heart, and hormone-producing organs.

Other possible complications include:

Not everyone develops these problems. Routine follow-up is intended to find complications before they cause major symptoms.

- Bilirubin gallstones and gallbladder inflammation
- Low bone density or fractures

- Blood clots, particularly after splenectomy
- Pulmonary hypertension, or high pressure in lung blood vessels
- Leg ulcers
- Areas of blood cell production outside the bone marrow
- Delayed puberty or other hormone problems
- Pregnancy-related worsening of anaemia

Prevention

Pyruvate kinase deficiency cannot be prevented because it is inherited.

Genetic counselling can explain inheritance, family testing, and reproductive options. Carrier testing may be useful for adult relatives or partners, especially when the family's PKLR gene changes are known. This does not prevent the gene change, but it can support informed decisions.

Complications can sometimes be reduced through regular monitoring. This may include checking iron levels, liver health, bone strength, and gallbladder symptoms. After splenectomy, recommended vaccinations and prompt assessment of fever help reduce infection risk.

Living with it and what to expect

Pyruvate kinase deficiency is lifelong. The gene changes do not disappear, but the day-to-day effects can change over time.

Many people develop a usual baseline for their energy and haemoglobin. Infections, surgery, pregnancy, or other physical stress can temporarily increase haemolysis and worsen anaemia. Recovery may take longer than it would for someone without the condition.

Some people lead active lives with periodic appointments and little treatment. Others need regular transfusions, iron-removing treatment, or help managing fatigue and complications. A mild haemoglobin reduction does not always mean mild symptoms, and severe-looking blood results do not affect everyone in the same way.

Long-term follow-up remains important even if anaemia feels manageable. Iron overload, gallstones, and bone changes can develop gradually and may not cause early symptoms.

Physical activity is often possible and beneficial, but your comfortable level may differ from someone else's. Pacing, rest, hydration, and adjustments during periods of increased anaemia

can help. Persistent fatigue deserves assessment because anaemia may not be the only cause.

Children may need practical support around school attendance, sports, or tiredness. Adults may need planning around work, travel, surgery, and pregnancy. Carrying information about the diagnosis, transfusion history, and spleen status can be useful when receiving unfamiliar medical care.

When to get medical help

Arrange routine follow-up with the team overseeing your condition. Contact them sooner if fatigue, jaundice, breathlessness, abdominal discomfort, or exercise tolerance is gradually worsening. New upper abdominal pain may need assessment for gallstones or spleen enlargement.

Seek urgent same-day medical advice for:

Call emergency services for severe difficulty breathing, chest pain, fainting, confusion, blue or grey lips, or signs of a severe allergic reaction during or after a transfusion.

A fever after splenectomy needs prompt assessment even if it initially seems mild. This is different from routine monitoring because serious infections can progress quickly without a working spleen.

- A sudden increase in weakness, pallor, jaundice, or dark urine
- Breathlessness that is new or clearly worse
- Severe or persistent upper abdominal pain
- Fever or signs of infection after splenectomy
- Symptoms suggesting a blood clot, such as one-sided leg swelling

Common questions

Is pyruvate kinase deficiency a type of cancer?

No. It is an inherited red blood cell enzyme condition. It does not involve uncontrolled cancer cell growth.

Can diet cure pyruvate kinase deficiency?

No diet can correct the PKLR gene changes or replace the missing enzyme activity. A balanced diet supports general health, but iron supplements should only be taken when testing confirms they are needed.

Why can I have too much iron if I am anaemic?

Anaemia means there are too few healthy red blood cells; it does not always mean the body lacks iron. Ongoing haemolysis can make the digestive system absorb extra iron, and transfusions add more iron. The body has no easy way to remove large excesses.

Will the condition get worse as I get older?

The underlying gene changes remain the same. Anaemia may stay relatively stable, but symptoms can fluctuate and complications may build up over years. Regular monitoring helps identify changes early.

Can I exercise with pyruvate kinase deficiency?

Many people can exercise, but anaemia may limit endurance. Increase activity gradually, rest when needed, and seek advice if exercise causes chest pain, fainting, or unusual breathlessness.

Can I pass pyruvate kinase deficiency to my children?

Yes, the PKLR gene change can be passed on. A child usually develops the condition only if they inherit a non-working copy from both biological parents. Genetic counselling can clarify the chance for a specific family.

Sources

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