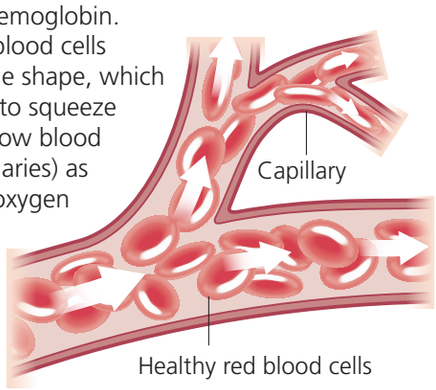
Understanding pyruvate kinase deficiency

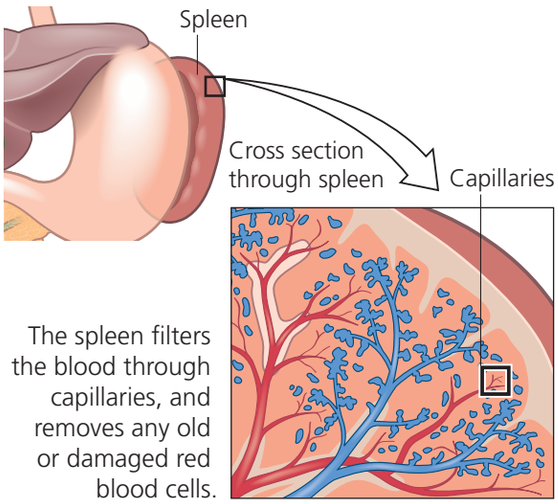
Pyruvate kinase (PK) deficiency is a rare genetic disease that affects red blood cells.

What do healthy red blood cells do?

Healthy red blood cells (erythrocytes) are produced in the bone marrow, and last for about **120 days.** Oxygen in the lungs binds to a molecule in red blood cells called hemoglobin. Healthy red blood cells have a flexible shape, which allows them to squeeze through narrow blood vessels (capillaries) as they deliver oxygen throughout the body.



What happens in the spleen?

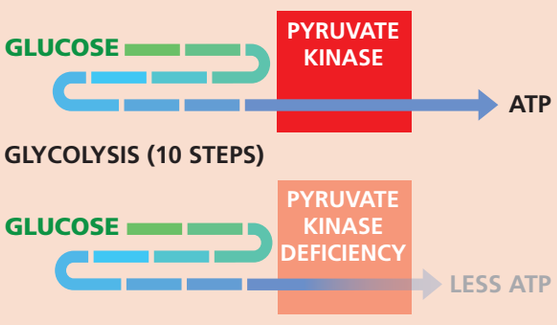


The spleen filters the blood through capillaries, and removes any old or damaged red blood cells.

How do red blood cells get energy?

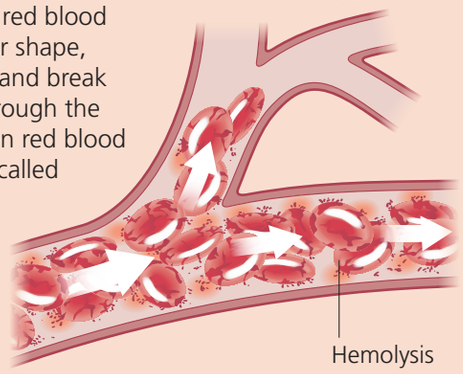
To stay flexible, red blood cells must keep their normal shape, and to do that they need energy. Red blood cells get their energy from a process called **glycolysis**, which turns glucose (a form of sugar) into a high-energy molecule called **ATP**.

Pyruvate kinase is responsible for the last step of this process. If a red blood cell has decreased amounts of pyruvate kinase, it cannot make enough ATP to hold its shape.



How does PK deficiency affect red blood cells?

Red blood cells that have decreased amounts of pyruvate kinase make less ATP, which means that they have less energy. With less energy, the red blood cells cannot hold their shape, become less flexible, and break apart as they pass through the spleen and liver. When red blood cells break apart it is called **hemolysis**. Because of hemolysis PK-deficient red blood cells only last for a few days or weeks.



The bone marrow continues to make new red blood cells (reticulocytes), but these are particularly susceptible to breaking apart in the spleen. The overall result is too few red blood cells, a condition called **anemia**.

Pyruvate kinase deficiency is a type of **hemolytic anemia**. Hemolytic anemia causes a decrease in hemoglobin and an increase in bilirubin.

How might PK deficiency affect me?

Signs and symptoms vary from person to person. The most common symptoms are:

Yellowing of the whites of the eyes (scleral icterus)

Yellowing of the skin (jaundice) and/or pale skin

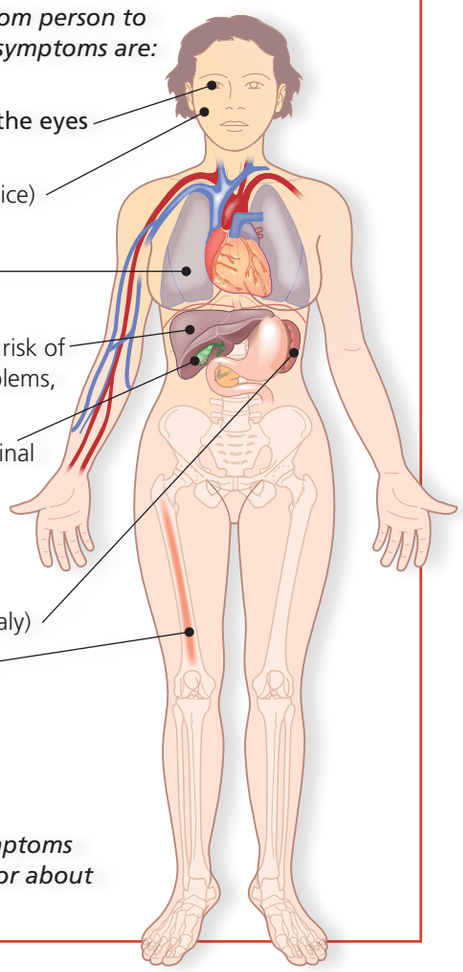
Tiredness (and less able to perform physical activity)

Too much iron increases the risk of liver, heart and hormone problems, and other complications

Gallstones may cause abdominal pain, nausea and vomiting

Enlarged spleen (splenomegaly)

Low bone strength



Less common signs and symptoms may occur so ask your doctor about any problems you have

How do you test for PK deficiency?

First, your doctor will take a **blood sample** to see if you have hemolytic anemia. Then, further blood tests will be carried out to find the cause of the hemolytic anemia.

Blood test findings of hemolytic anemia

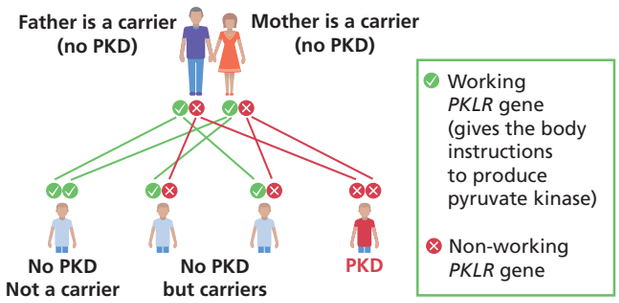
- Decreased hemoglobin or hematocrit (red blood cells)
- Increased reticulocytes (young red blood cells)
- Increased bilirubin from breakdown of red blood cells

Blood tests that confirm PK deficiency

- Low pyruvate kinase enzyme activity
- Genetic test that shows 2 mutations in the *PKLR* gene

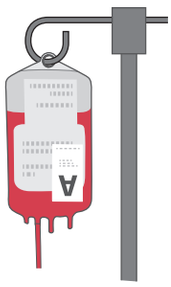
How did I inherit PK deficiency?

PK deficiency is an **inherited autosomal recessive disease**. To inherit the condition you have to receive two copies of a non-working *PKLR* gene (one from each parent).



How can PK deficiency be treated?

At present there is no drug available to treat PK deficiency, but your symptoms can be managed. The type of supportive treatment you receive depends on how the disease affects you.



Blood transfusions are given if you have symptoms of anemia. They increase the hemoglobin level.

Some patients never need to have a transfusion. Some have only a few transfusions, and others have frequent transfusions.

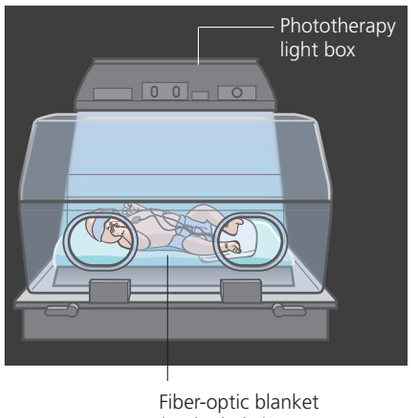
Special circumstances that often need transfusion include:

- **Hemolytic crisis** – a worsening of hemolytic anemia caused by infections, stress or pregnancy.
- **Aplastic crisis** – a temporary halt in new red blood cell production caused by parvovirus infection (Fifths disease), which causes a temporary severe anemia and then self-resolves.

With or without blood transfusions, PK deficiency can lead to too much iron in the body. Patients need regular monitoring for **iron overload** through blood tests (a ferritin test) or radiology scans. Iron overload can be treated with medications (chelation therapy) or blood draws (phlebotomy).

High levels of bilirubin cause **jaundice** (yellowing of the skin) in children and adults. Newborns can develop complications of the nervous system related to jaundice. Fluorescent light decreases bilirubin, so newborns are often treated with **phototherapy.**

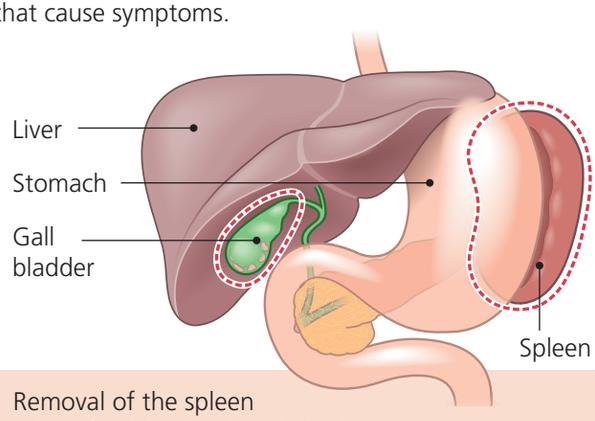
Or they may receive **exchange transfusion** in which an amount of blood is removed and replaced with transfused blood.



Removal of the spleen (splenectomy) increases hemoglobin levels in most patients with PK deficiency, improving anemia and reducing the need for transfusions. Without a spleen, young red blood cells survive longer and the reticulocyte count increases.

After the spleen is removed, the anemia improves but hemolysis continues.

The gallbladder may be removed (cholecystectomy) at the same time as the spleen or if you have gallstones that cause symptoms.



Removal of the spleen raises the risk of serious infections, such as sepsis (bacteria in the bloodstream) or meningitis, and increases the risk of blood clots.

Your doctor may recommend:

- Regular antibiotics after surgery to prevent infection.
- Additional (non-routine) vaccinations before and after the operation.
- Medications after surgery to prevent blood clots.

If you have had your spleen removed and develop a fever at any time, see your doctor or go to the emergency department for laboratory tests and broad spectrum antibiotics IMMEDIATELY.

Other treatments

Calcium and vitamin D supplements may help to support bone health.

A few patients with PK deficiency have had a **bone marrow (stem cell) transplantation**, which can cure PK deficiency but is associated with severe risks.

Potential new therapies are currently being studied.

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