# Pyruvate Kinase Deficiency

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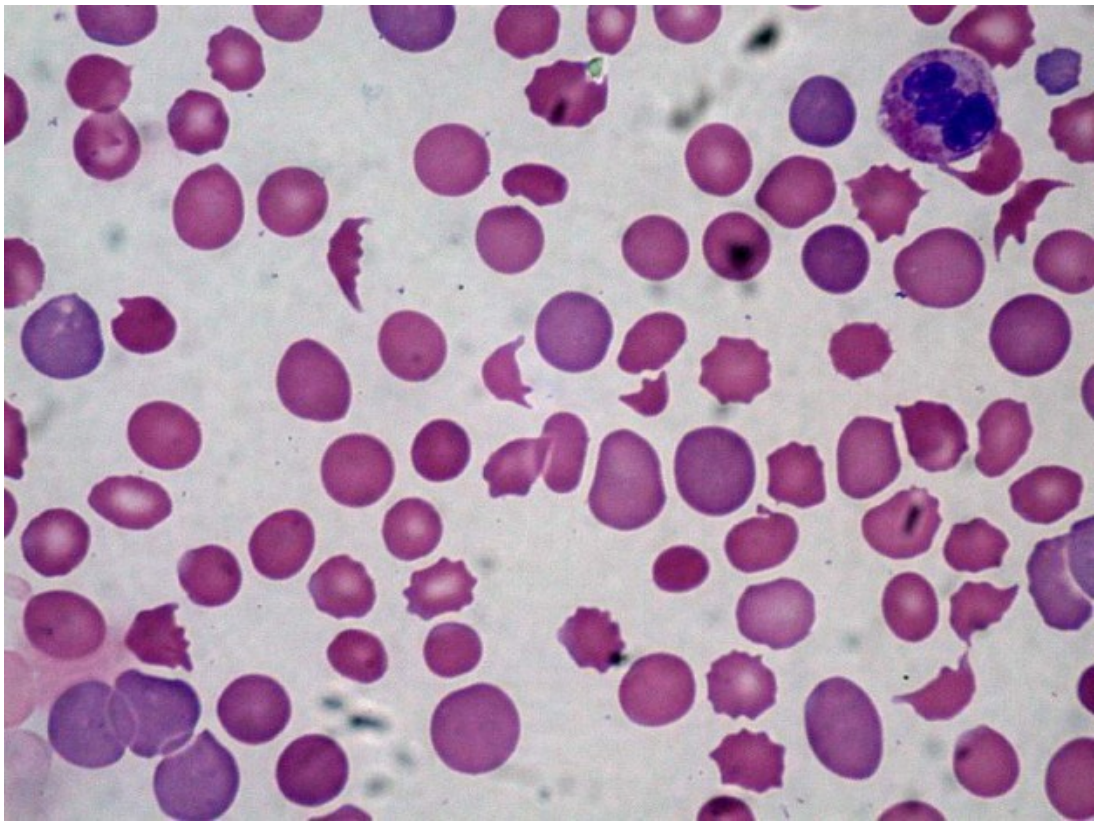
**In this article, the rare disease pyruvate kinase deficiency is presented, emphasizing on their etiology and clinic.**

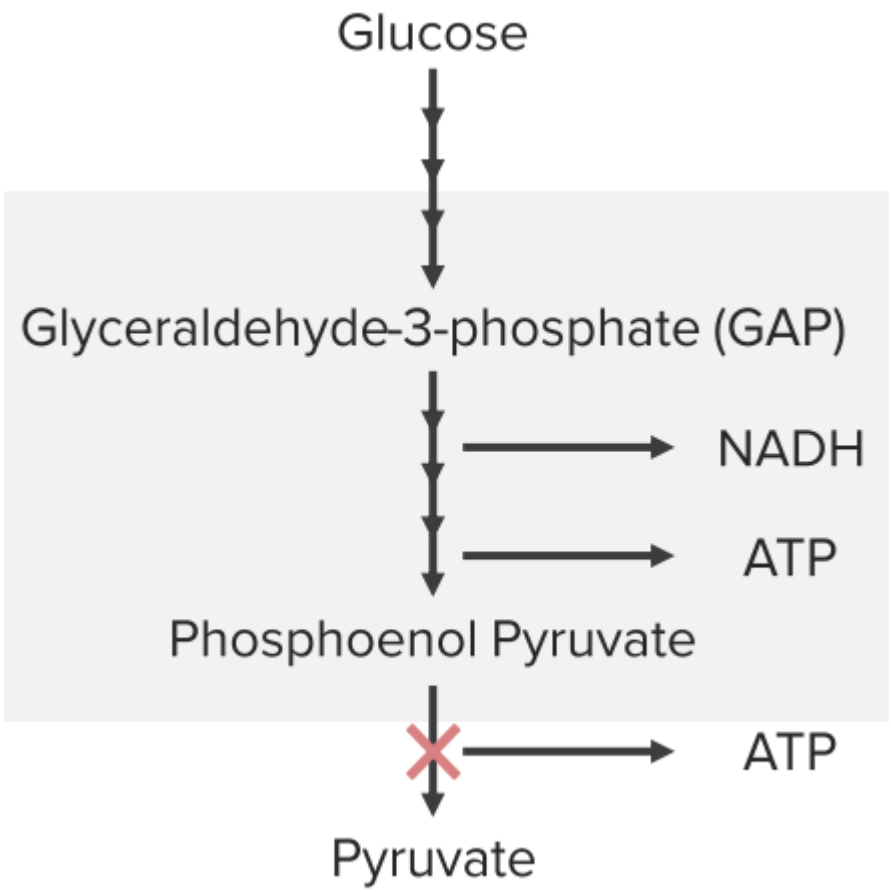


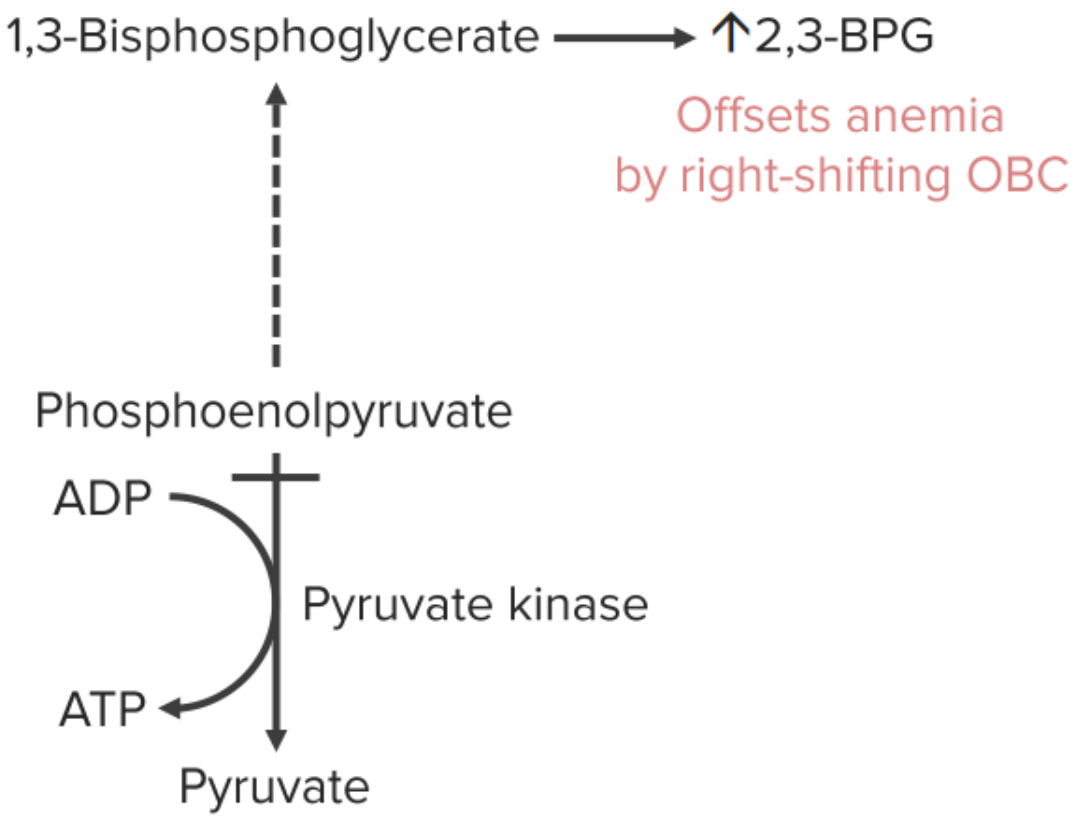
## Definition and Etiology of Pyruvate Kinase Deficiency

The pyruvate kinase (PK) defect is more commonly inherited in an **autosomal recessive** pattern, even though both autosomal dominant and recessive forms of inheritance have been observed. Due to decreased ATP synthesis, the erythrocytes lose their physiological flexibility and become rigid. It is the second most common cause of enzyme-deficient hemolytic anemia, following glucose-6-phosphate dehydrogenase deficiency.

## Etiology of Pyruvate Kinase Deficiency

PK is the last enzyme in glycolysis. PK deficiency is caused by gene mutations that decrease its activity.


Glucose
Glyceraldehyde-3-phosphate (GAP)
NADH
ATP
Phosphoenol Pyruvate
ATP
Pyruvate

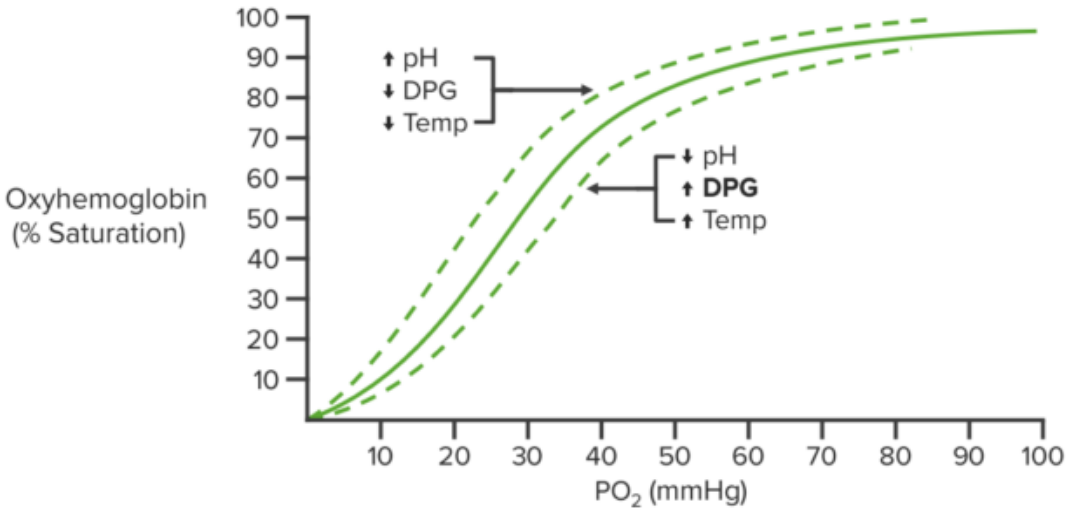

1,3-Bisphosphoglycerate
↑2,3-BPG
Offsets anemia
by right-shifting OBC
Phosphoenolpyruvate
ADP
Pyruvate kinase
ATP
Pyruvate

## Clinical Symptoms and Diagnosis of Pyruvate Kinase Deficiency

Usually, the symptoms associated with PK deficiency are less distinct. In addition to jaundice and gallstones, skeleton deformations can occur (frontal bumps). The blood smear reveals poikilocytes.

The RBCs use only glycolysis to generate energy due to the absence of mitochondria. In PK deficiency, therefore, there is limited ATP or NADH production. ATP deficiency affects the $NA^{+}/K^{+}$ ATPase, leading to osmotic instability and deformed RBCs that are cleared in the spleen (extravascular hemolysis).

NADH deficiency decreases the reducing power required to convert methemoglobin ($Hb\text{-}Fe^{3+}$) to hemoglobin ($Fe^{2+}$). Because of the distal block, 2,3-BPG levels are increased. The 2,3-BPG binds to hemoglobin and alters its confirmation via allosteric inhibition, shifting the oxygen saturation curve to the right.




Defects associated with PK are usually diagnosed in childhood as chronic hemolytic anemia. The serum methemoglobin is elevated. Although PK deficiency is most common in glycolysis, it is still a very rare disease.

## Treatment of Pyruvate Kinase Deficiency

Splenectomy provides only symptom relief. No definitive cure is available.

## References


Miwa, S., &Fujii, H. (1990). Pyruvate kinase deficiency. *Clinical Biochemistry*, *23*(2), 155-157. doi:10.1016/0009-9120(90)80029-i

Pyruvate Kinase Deficiency. (2008). *Encyclopedia of Genetics, Genomics, Proteomics and Informatics*, 1608-1608. doi:10.1007/978-1-4020-6754-9_13890

Pyruvate kinase deficiency. Association with G6PD deficiency. (1992). *BMJ*, *305*(6856), 760-762. doi:10.1136/bmj.305.6856.760

Zanella, A. (2016). *Pyruvate kinase deficiency*. London: Henry Stewart Talks.

Notes