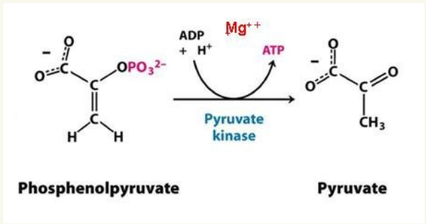
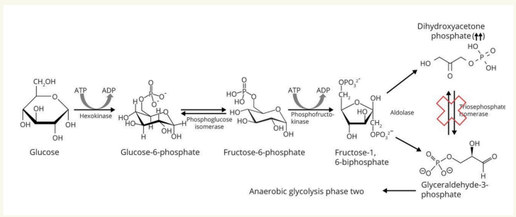
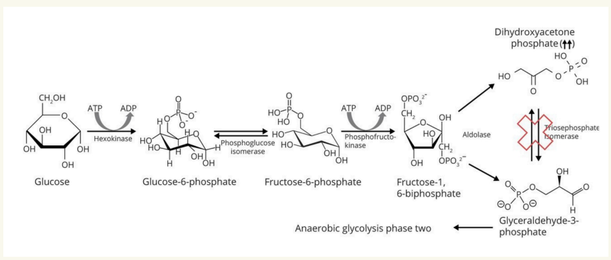
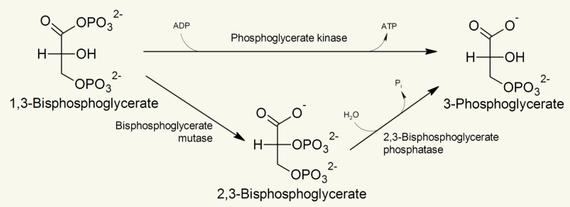
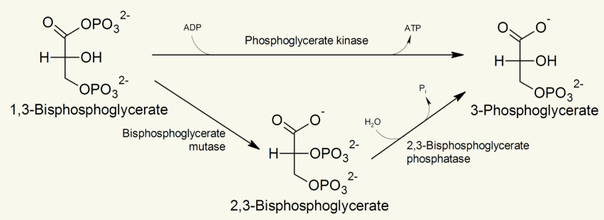
enzymes deficiencies related to RBC metabolism

	reaction of enzyme	intermediates & products	symptoms & clinical picture / slides
Pyruvate kinase deficiency	 aim to produce ATP , so problems related to decrease in ATP	- no intermediates here , but you have to know that if ATP production decreased then hemolysis occur . - these deficiencies caused by gene mutations - More than 180 gene mutations in had been reported to be associated with PK deficiency. - **Most of these mutations (70%) are the missense mutants** c.1456C→T(Arg486Trp), c.1529G→A (Arg510Gln), c.994G→A (Gly332Ser), and **the nonsense mutant c.721G→T (Glu241stop).**	**Pyruvate kinase deficiency**: - It is one of the most common enzymopathy associated with chronic hemolytic anemia, which usually occurs in compound heterozygotes for two different mutant alleles and in homozygotes. - The increased 2, 3-BPG levels eases the anemia by lowering the oxygen-affinity of hemoglobin. - Phenotypically, the clinical picture varies from severe hemolysis causing neonatal death, to a well-compensated hemolytic anemia and only very rare cases can present with hydrops fetalis.
Triose phosphate isomerase deficiency	 reaction aim to convert DHAP into GAP , so deficincy in it lead to: **low ATP and DHAP effects**	✅ **high levels of dihydroxyacetone phosphate (DHAP)** ❌ **relatively minute decrease of ATP.**	- Dihydroxyacetone phosphate accumulation has been reported to be toxic for cellular functions and responsible for the severity of TPI enzymopathies but its mechanism of toxicity is not well understood. - The defect leads to hemolytic anemia coupled with neurological dysfunction.
Phosphoglucose isomerase deficiency	 reaction aims to convert G6P into F6P which are important step in glycolysis , so deficincy in it lead to low ATP and hemolysis , also increase production of G6P which lead to shunt into PPP (pentose phosphate pathway) and increase in PPP .	With the effect of hexokinase inhibition, **ATP, D23PG and GSH regeneration decreases.** **GSH = reduced glutathion** **decrease in it = high oxidstive stress = ⬆️ hemolysis**	**Phosphoglucose isomerase deficiency** - Phosphoglucose isomerase catalyzes the reversible isomerization from G6P to F6P, an equilibrium reaction of glycolysis. - Glucose turnover reacts, therefore, only on deficiency below a very low critical residual activity of PGI but then with a decline of lactate formation, i.e., decrease in glycolytic flux. - The consequence of a limitation by the PGI reaction is an increase of the G6P level which causes a feedback inhibition of hexokinase resulting both in a lower rate of glycolysis and increased PPP activity associated, in turn, with the recombination of F6P formed in PPP with glycolytic pathway. - With the effect of hexokinase inhibition, ATP, D23PG and GSH regeneration decreases. - This is the third most common enzymopathy in the world.
Diphosphoglycerate mutase deficiency	 reaction aims to convert 1,3 BPG into 2,3 BPG .. so it is very important in rubobort leubiring shunt . deficincy in it lead to decrase 2,3 BPG production 👉 high O2 affinity and low cellular oxygenation	✅ **ATP, FDP, triose phosphates, P3G, P2G, PEP are enhanced.** ❌ **ADP, D23PG, F6P, G6P are diminished.**	**Diphosphoglycerate mutase deficiency** - Disphosphoglyceromutase is a multifunctional enzyme which catalyzes both the synthesis and dephosphorylation of D23PG in human red blood cells. - With lowering of disphosphoglyceromutase, the turnover via D23PG declines in favor of substrate phosphorylation catalyzed by phosphoglycerate kinase and pyruvate kinase leading to changes of the metabolic pattern. ATP, FDP, triose phosphates, P3G, P2G, PEP are enhanced, ADP, D23PG, F6P, G6P are diminished.
Phosphoglycerate kinase deficiency	 reaction aims to prduce 3-PG and continue in glycolytic pathway . **deficincy in it lead to accumulation of 1,3 DPG which activate Rabobort Leubering Shunt and increase in 2,3 BPG**	✅ **significant accumulation of D23PG** ❌ **decreased concentration of ATP**	**Phosphoglycerate kinase deficiency** - PGK is a key enzyme for ATP generation in the glycolytic pathway, catalyzing the conversion of 1,3-diphosphoglycerate to 3-phosphoglycerate bypassing the Rapoport-Luebering shunt. - A significant accumulation of D23PG, and a decreased concentration of ATP were observed in patients with PGK deficiency. - Also, diminished glucose consumption was reported.