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Disorders of the Pentose Phosphate Pathway

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- **Three inborn errors in the pentose phosphate pathway are known.**
- **In glucose-6-phosphate dehydrogenase deficiency, there is a defect in the first, irreversible step of the pathway. As a consequence NADPH production is decreased, making erythrocytes susceptible to oxidative stress. Drug-and fava bean-induced haemolytic anaemia is the main presenting symptom of this defect.**

- **Deficiency of ribose-5-phosphate isomerase has been described in one patient who suffered from a progressive leucoencephalopathy and developmental delay.**
- **Transaldolase deficiency has been diagnosed in three unrelated families. All patients presented in the newborn period with liver problems.**

- **Essential pentosuria, due to a defect in the enzyme xylitol dehydrogenase, affects the related glucuronic acid pathway. Whereas the pentose phosphate pathway involves D stereoisomers, glucuronic acid gives rise to L-xylulose which is subsequently converted into xylitol and D-xylulose. Affected individuals excrete large amounts of L-xylulose in urine.**

Ribose-5-Phosphate Isomerase Deficiency

Genetics

The presence of two mutant alleles in the ribose-5-phosphate isomerase gene with one of these in the patient's mother (the father could not be investigated) suggest autosomal recessive inheritance.

Metabolic disorders

Ribose-5-phosphate isomerase deficiency is a block in the reversible part of the pentose phosphate pathway. In theory, this defect leads to a decreased capacity to interconvert ribulose-5-phosphate and ribose-5-phosphate and results in the formation of sugars and polyols: ribose and ribitol from ribose-5-phosphate and xylulose and arabitol from ribulose-5-phosphate via xylulose-5-phosphate.

Transaldolase Deficiency

Transaldolase deficiency has been diagnosed in 3 families. Clinical symptoms among these families vary, but liver disease has been present in all.

Genetics

- **The same mutation was found in the first and third families, but was different in the second family. All patients were homozygous for these specific mutations, suggesting autosomal recessive inheritance.**

Metabolic Defects

Transaldolase, located in the reversible part of the pentose phosphate pathway, recycles pentose phosphates into hexose phosphates in concerted action with transketolase. Its deficiency results in the accumulation of polyols derived from the pathway intermediates: erythritol, arabitol and ribitol.