Disorders of creatine synthesis

- The synthesis of creatine occurs in two steps:

1. Reaction catalyzed **by L-argininglycinamide diffease (AGAT)** – transfer of the amidine group from arginine to glycine to form guanidinoacetate
2. Raction catalyzed **by guanidin acetate methyl transformerase (GAMT)** – methylation of the amidine group of the guanidinoacetate molecule by the action of S-adenosylmethionine N-guanidinoacetate methyltransferase

- The synthesis of creatine takes place mainly in the kidneys and pancreas, which have high AGAT activity, and then in the liver, which have high GAMT activity.
- Creatine from these organs gets through the blood to the organs where it is used (mainly muscles and brain)
- When creatine enters tissue utilization, the human form of Cl-dependent creatine carrier (CRTR), **SLC6A8**
- Part of the intracellular creatine is reversibly converted to high-energy creatine phospahte by the action of creatine kinase (CK), which exists in three cytosol isoforms, the brain type BB-CK, the muscle type MM-CK and the heterodimer MB-CK creatine phosphate turn into creatinine non-enzymate in the muscle

Creatine synthesis disorders

- Common features are mental retardation, speech delay and epilepsy due to creatine deficiency in the brain
  - They are diagnosable magnetic resonance spectroscopy of the brain, then in the blood, urine and amniotic fluid

  - **L-argininglycinamide aminotransferase deficiency (AGAT)**
  - **Guanidine acetate deficiency methyltransferase (GAMT)** – guanidinoacetate accumulates, the most severe clinical manifestations, convulsions, extrapyramidal symptoms
  - **SLC6A8** deficiency - increased creatine/creatinine ratio

Inheritance:

- AGAT and GAMT deficit are autosomal recessive inherited
- SLC6A8 deficiency is X-linked hereditary

Treatment:

- Oral creatine supplementation in the form of creatine monohydrate in AGAT and GAMT deficiency
- Dietary restriction of arginine in GAMT deficiency
- In patients with SLC6A8 deficiency, no effective treatment has yet been found, the application of extremely high doses of creatine is being tried, glycine and arginine are also administered.

Links

Literature

- FERNANDES, John. *Diagnosis and treatment of hereditary metabolic disorders.* 1st edition. Praha : Triton, 2008. s. 576-580. ISBN 978-80-7387-096-6.