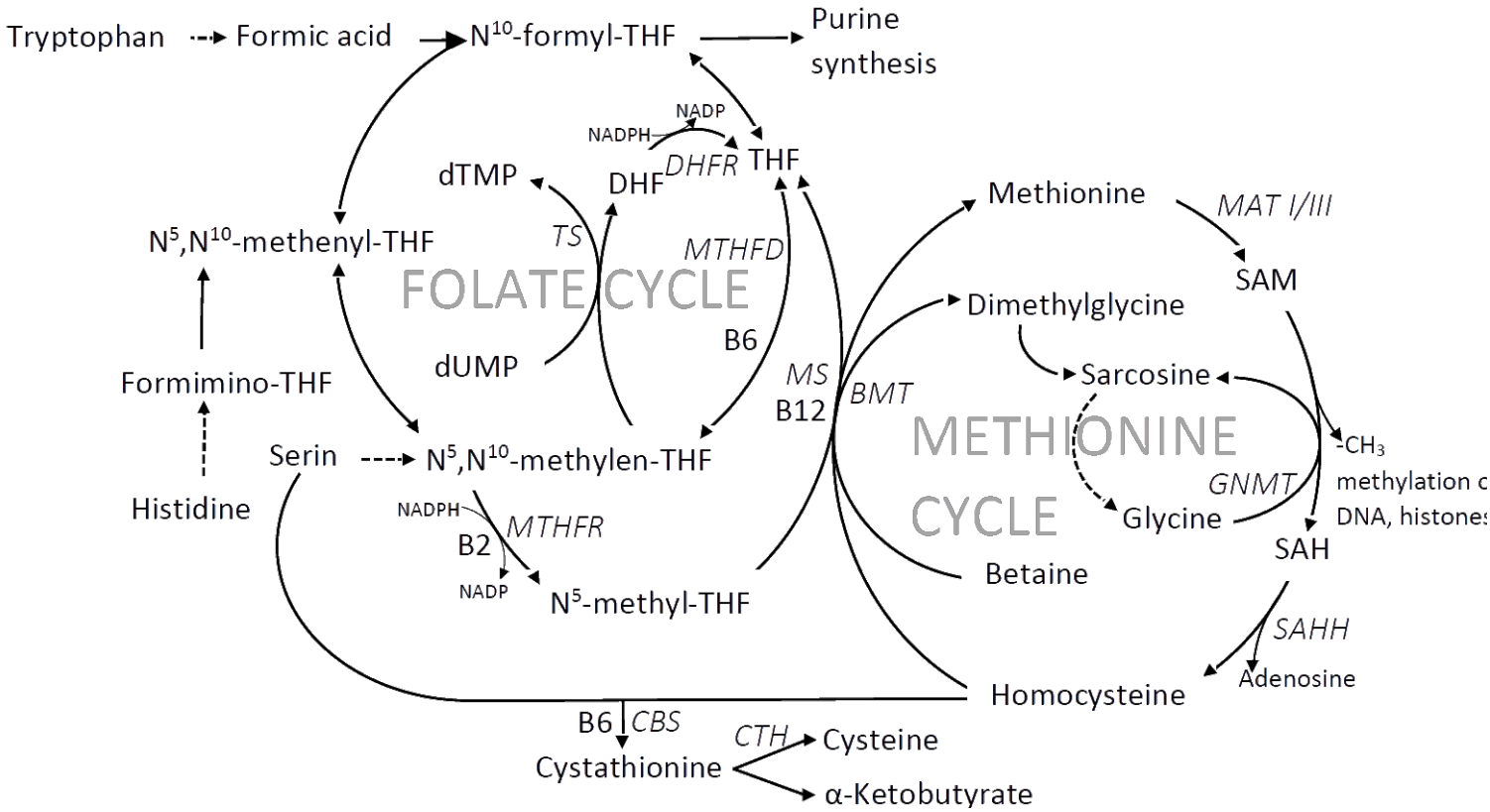
# Disorders of sulfur amino acid metabolism

## Congenital disorders of sulfur AMK metabolism




- sulphur AMKs include methionine, homocysteine, homocystin, cystathionine, cysteine, cystine

### Remethylating homocystinuria

- defects in which homocysteine cannot be converted to methionine
- approx. 10 diseases - most often deficiency
- Rarely disorders of methionine adenosyltransferase I / III, glycine N-methyltransferase, S-adenosylhomocysteine hydrolase and adenosine kinase
- '*clinical picture*: severe myelination disorders, neurological manifestations, thrombosis
- **laboratory**: higher Hcy, low Met and SAM
- **therapy**: betaine, methionine, SAM

### Homocystinuria

- AR hereditary
- frequency 1 : 200,000[1]

- disruption of β-cystathionine synthetase activity (catalyzes the formation of cystathion from homocysteine and serine)
- **clinical picture**: the manifestations are not obvious immediately after birth, but in further development there are symptoms affecting various tissues and organs
  - they appear in toddler or preschool age - a disorder of mental development (psychomotor retardation in 60% of cases[2]), marfanoid phenotype (tall slender stature, arachnodactyly, kyphosis, scoliosis, osteoporosis),glaucoma and central and peripheral thromboembolic events,
  - dislocations of lenses cause strong myopia, thromboses occur most often at the base of the skull and are life-threatening. Thanks to thrombosis, gangrene of the organs occurs, which usually ends the patient's life in the 20s-30s. a year
  - atrophy of the optic nerve, cor pulmonale, hypertension
- **laboratory**: increased homocysteine and methionine in the blood, frequent metabolic osteopathy
  - must be confirmed at the enzymatic and molecular level
- **dif.dg**: homocysteinemia is also present with - disorders of the metabolism of methylmalonic acid, cobalamin or with B6 deficiency
- **therapy**: some patients (approx. 50%[2]) respond favorably to high doses of pyridoxine (vit B6) (in the amount of 300-900 mg/ d[2]), which is a cofactor of β-cystathionine synthetase
  - in case of complete lack of enzymatic activity, it is necessary to start dietary treatment with limited supply of methionine and supply of cystine
  - [[prenatal diagnosis] is available

### Cystinosis

- AR hereditary
- frequency 1 : 50,000 - 1 : 1,000,000[2]
- 3 subtypes according to phenotype
  - nephropathic cystinosis
  - intermediate cystinosis
  - non-nephropathic or ocular cystinosis

- this is a defect in the lysosomal transport of cystine, which leads to its storage
- accumulation affects the RES (spleen, liver, nodes and bone marrow), deposits can also be demonstrated in the cells of the kidney tubules (primarily proximal) and conjunctiva
- clinical manifestations are visible only in the kidneys, where there is a severe violation of their function
- '*laboratory*: ***manifestations of kidney damage and their prox. tubule – glycosuria, phosphaturia, albuminuria, hyperaminoaciduria, chronic acidosis and uremia together is called proximal tubular syndrome or also*** *Fanconi syndrome.* '
  - all aminoaciduria is due to gradual impairment of GF (glomerular filtration), which soon results in kidney failure
- **clinical picture:** in the second half of the first year there is **polydipsia, polyuria, dehydration, metabolic acidosis, photophobia and hypophosphatemic rickets**'
- **therapy**: symptomatic treatment of tubular dysfunction (supply of electrolytes and fluids), usually high doses of vitamin D are necessary (increase in intestinal phosphate absorption and decrease in urinary phosphate excretion)[2]
  - by administration of cysteamine, which works in two ways
    - by binding to cystine, it creates cysteine, which can be excreted from the lysosome using the cysteine transporter[2]
    - by binding to cystine, cysteine-cysteamine disulfide is formed, which can be excreted from the lysosome by means of the lysine transporter[2]
  - **diagnosis:** can be determined by examining the eyes, as cystine crystals are also deposited in the cornea and is further proven biochemically by determining the concentration of cystine in leukocytes or cultured fibroblasts, which is increased 50-100 times.

### Cystinuria

- AR hereditary
- frequency 1 : 2000 - 1 : 7000[2]
- congenital disorder of the transport of **dibasic AMKs -'**cystine, *lysine, ornithine and arginine in kidney tubules and in the intestine*
- **clinical picture: cystine nephrolithiasis, which is caused by the poor solubility of cystine in water and further by its crystallization in an acidic environment**
- '*diagnosis*: increased levels of cystine, ornithine, arginine, lysine in urine; kidney and excretory system[2]
- **therapy**: the aim is to prevent nephrolithiasis and therefore a high fluid intake (4-5l) combined with night drinking is recommended
  - only in severe cases it is possible to consider drug therapy with D-penicillamine (as the treatment has many side effects) or mercaptopropionylglycine, which causes the formation of more soluble bisulfides with cystine[2]

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Kategorie:Vložené články Kategorie:Patobiochemie Kategorie:Pediatrie

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2. {{#switch: book |book = *Incomplete publication citation.* MUNTAU, Ania Carolina. *Pediatrics*. Prague : Grada, 2009. 581 s. pp. 104-105. 978-80-7262-438-6. |collection = *Incomplete citation of contribution in proceedings*. MUNTAU, Ania Carolina. *Pediatrics.* Prague : Grada, 2009. 581 s. pp. 104-105. {{ #if: 978-80-247-2525-3 |978-80-7262-438-6} } |article = *Incomplete article citation.* MUNTAU, Ania Carolina. 2009, year 2009, pp. 104-105, |web = *Incomplete site citation*. MUNTAU, Ania Carolina. Grada, ©2009. |cd = *Incomplete carrier citation*. MUNTAU, Ania Carolina. Grada, ©2009. |db = *Incomplete database citation.* Grada, ©2009. |corporate_literature = MUNTAU, Ania Carolina. *Pediatrics.* Prague : Grada, 2009. 581 s. 978-80-7262-438-6} }, s. 104-105.