



State of CT Genetics Newborn Screening Program Health Professional Fact Sheet

Homocystinuria

Homocystinuria (HCU) is a defect in the catabolism of sulfur-containing amino acids. The most common cause of HCU is a deficiency of the enzyme cystathionine B-synthase. Elevated levels of homocysteine, methionine, and metabolites of homocysteine accumulate in the blood and urine of these patients. Screening in Connecticut was instituted in 1993.

GENETIC BASIS

- Autosomal recessive condition—Recurrence risk is 25%
- Prenatal diagnosis is possible

CT PREVALENCE 1:50,000 to 150,000

CLINICAL FEATURES OF UNTREATED DISEASE

Severity

- Physical disabilities: Marfanoid habitus, ectopia lentis, glaucoma, cataracts, osteoporosis with bone deformities, high palatal arch, and muscle weakness with a shuffling gait
- Developmental disabilities: mental retardation, developmental delay is reported in 65% to 80% of untreated individuals
- Mortality: frequently due to thromboembolism in cerebral, pulmonary, renal, and myocardial circulation. Death usually occurs within the first year of life. Death can also occur later from thromboembolism.

Symptomatic diagnosis

A symptomatic diagnosis is limited due to nonspecific features during the newborn period. Ocular abnormalities, because of their distinctive lens displacement, may be the only symptoms leading to an early clinical diagnosis.

Variants

There are several forms of HCU that are characterized by normal or low blood levels of methionine and the absence of ocular abnormalities. These variants are additional disorders of methionine metabolism, including decreased N5 methyltetrahydrofolate homocysteine methyltransferase activity due to vitamin B12 deficiency and decreased N5, 10 methyl tetrahydrofolate reductase activity.

CLINICAL OUTCOME WITH SCREENING AND TREATMENT

Mortality

Treatment seems to reduce the risk of thromboembolic episodes.

Clinical Disability

The incidence of mental retardation may be prevented or reduced. Ectopiltentis seems to be delayed, and the incidence of seizures is reduced.

Variability

Clinical variability remains despite therapy. Not all affected individuals have elevated methionine levels.

Interventions

Approximately 10-15% of patients respond to large doses of vitamin B6. Nonresponsive patients with cystathionine B-synthase deficiency must be treated with a methionine-restricted, cystine-supplemented diet. Many patients receive betaine in addition to dietary restrictions. A nutritionist and metabolic specialist must coordinate therapy.

SCREENING FOR HCU

Laboratory tests

- The test for elevated blood methionine content on filter paper blood specimen using a Tandem Mass Spectrometer.

POSITIVE TEST RESULTS

- The primary care provider is notified by the DPH, Genetic NBS Tracking Unit nurse consultant.
- A referral is made by the DPH, Genetic NBS Tracking Unit nurse consultant to one of the Genetic Regional Treatment Centers.
- The primary care provider will be advised by the DPH, Genetic NBS Tracking Unit nurse consultant to contact the Genetic Regional Treatment Center to make a prompt referral and arrange for confirmation testing and evaluation.

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