

**Disease Name:**

**HOMOCYSTINURIA**

CYSTATHIONINE BETA-SYNTHASE DEFICIENCY, CBS DEFICIENCY,  
HOMOCYSTINURIA, PYRIDOXINE-RESPONSIVE

**Classification:** Sulfur amino acid disorder

**Genetic Information:**

**Inheritance:** Autosomal Recessive

**Population Incidence:** 1:100,000

**Ethnic Incidence:** Northern European, Ireland 1:65,000

**Gene & Location:** 21q22.3

**Common Mutation:** Several; >130 mutations known

**OMIM #** 236200

**Disease Information:**

**Symptom Onset:** Early to late childhood

**Symptoms:** Mental retardation in 66%, psychiatric disorders in 50%. Ectopia lentis (dislocated lenses) in 80%, Marfanoid body habitus with limited joint mobility and generalized osteoporosis. Major risk of thrombosis in childhood if there is also a mutation in factor V Leiden. Pneumothoraces, hypopigmentation and pancreatitis have also been reported.

**Physical Findings:** Newborns will be asymptomatic and non-dysmorphic. Older children will have mental retardation, dislocated lenses, Marfanoid body habitus and osteoporosis.

**Treatment:** Approximately 50% of patients are pyridoxine (B6) responsive and may not need additional treatment. For non-responders therapy consists of a low methionine diet, supplemented with cystine and Betaine to lower plasma disulfide metabolites. Vitamin C has been shown to have a beneficial effect on endothelial dysfunction and may be considered as an adjunct therapy to reduce the risk of thrombosis.

**Natural History without treatment:** Mental retardation or reduced IQ in 66%, psychiatric disorders, dislocated or subluxed lenses. Marfanoid body habitus with osteoporosis and limited joint mobility. Stroke with disability may occur by age 15 in 12-27% of patients. Offspring of homocystinuric mothers are normal regardless of the mother's biochemical control.

**Natural History with treatment:** Infants treated from birth with good biochemical control of methionine develop normally.

