Homocystinuria

Description

Homocystinuria is an inherited disorder in which the body is unable to process certain building blocks of proteins (amino acids) properly.

The most common form of homocystinuria, called classic homocystinuria, is characterized by tall stature, nearsightedness (myopia), dislocation of the lens at the front of the eye, a higher risk of blood clotting disorders, and brittle bones that are prone to fracture (osteoporosis) or other skeletal abnormalities. Some affected individuals also have developmental delay and learning problems.

Less common forms of homocystinuria can cause intellectual disability, slower growth and weight gain (failure to thrive), seizures, and problems with movement. They can also cause and a blood disorder called megaloblastic anemia, which occurs when a person has a low number of red blood cells (anemia), and the remaining red blood cells are larger than normal (megaloblastic).

The signs and symptoms of homocystinuria typically develop during childhood, although some mildly affected people may not show signs and symptoms until adulthood.

Frequency

Classic homocystinuria affects at least 1 in 200,000 to 335,000 people worldwide. The disorder appears to be more common in some countries, such as Ireland (1 in 65,000), Germany (1 in 17,800), Norway (1 in 6,400), and Qatar (1 in 1,800). The rarer forms of homocystinuria each have a small number of cases reported in the scientific literature.

Causes

Variants (also called mutations) in the *CBS*, *MTHFR*, *MTR*, *MTRR*, and *MMADHC* genes cause homocystinuria.

Variants in the *CBS* gene cause classic homocystinuria. The *CBS* gene provides instructions for making an enzyme called cystathionine beta-synthase. This enzyme helps break down the amino acid methionine. Specifically, this enzyme is responsible for converting the amino acid homocysteine to a molecule called cystathionine. Variants in the *CBS* gene disrupt the function of cystathionine beta-synthase, preventing homocysteine from being used properly. As a result, homocysteine and methionine

build up in the blood. Some of the excess homocysteine is excreted in urine.

Rarely, homocystinuria can be caused by variants in several other genes. The enzymes made by the *MTHFR*, *MTR*, *MTRR*, and *MMADHC* genes play roles in converting homocysteine to methionine. Variants in any of these genes prevent the enzymes from functioning properly, which leads to a buildup of homocysteine in the body. Researchers have not determined how excess homocysteine and related compounds lead to the signs and symptoms of homocystinuria.

Learn more about the genes associated with Homocystinuria

- CBS
- MMADHC
- MTHFR
- MTR
- MTRR

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell must have a variant to cause the disorder. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

Although people who carry one altered copy and one normal copy of the *CBS* gene do not have homocystinuria, they are more likely than people without a *CBS* variant to have shortages (deficiencies) of vitamin B12 and folic acid.

Other Names for This Condition

- Cystathionine beta synthase deficiency
- Homocysteinemia

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Classic homocystinuria (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0751202/)
- Genetic Testing Registry: Homocystinuria (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0019880/)
- Genetic Testing Registry: Homocystinuria due to methylene tetrahydrofolate reductase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1856058/)
- Genetic Testing Registry: Homocystinuria, cblD type, variant 1 (https://www.ncbi.nl

m.nih.gov/gtr/conditions/C1848553/)

Genetic and Rare Diseases Information Center

- Homocystinuria (https://rarediseases.info.nih.gov/diseases/10770/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Homocystinuria%22)

Catalog of Genes and Diseases from OMIM

- HOMOCYSTINURIA DUE TO CYSTATHIONINE BETA-SYNTHASE DEFICIENCY (https://omim.org/entry/236200)
- HOMOCYSTINURIA DUE TO DEFICIENCY OF N(5,10)-METHYLENETETRAHYDROFOLATE REDUCTASE ACTIVITY (https://omim.org/entry/236250)
- HOMOCYSTINURIA-MEGALOBLASTIC ANEMIA, cblE COMPLEMENTATION TYPE; HMAE (https://omim.org/entry/236270)
- METHYLMALONIC ACIDURIA AND HOMOCYSTINURIA, cblD TYPE; MAHCD (https://omim.org/entry/277410)
- HOMOCYSTINURIA-MEGALOBLASTIC ANEMIA, cblG COMPLEMENTATION TYPE; HMAG (https://omim.org/entry/250940)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(Homocystinuria%5BMAJR%5D)+AND+(homocystinuria%5BTIAB%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3000+days%22%5Bdp%5D)

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Last updated May 1, 2023