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What is Homocystinuria, CBS-related?

Homocystinuria, CBS-related is an inherited metabolic disease characterized by developmental delays, eye problems, skeletal abnormalities, and increased risk of blood clots. It involves abnormalities in the enzyme cystathionine beta-synthase (CBS) that breaks down the amino acid homocysteine. Symptoms are believed to be due to the toxic build-up of homocysteine and its metabolites in the body.[1] Homocystinuria, CBS-related is also referred to as "classical homocystinuria." [2]

What are the symptoms of Homocystinuria, CBS-related and what treatment is available?

Homocystinuria, CBS-related is a disease that varies in severity and age at onset, even within families. Many individuals show symptoms in early childhood, while others may have a blood clot in adulthood as their first sign. Symptoms of homocystinuria, CBS-related may include[3]:

- Developmental delays/mental retardation
- Ectopic lentis (dislocation of the lens of the eye)
- Myopia (nearsightedness)
- Skeletal abnormalities (excessive height and length of the limbs)
- Risk for osteoporosis (low bone density) at an early age
- Thromboembolism (blood clots)
- Seizures
- Psychiatric problems

There is no cure for homocystinuria, CBS-related. Treatment includes a low protein diet and nutrition supplements, including vitamin B_6. When started early in infancy, treatment may minimize or prevent mental retardation and other complications of the disease. Two forms of homocystinuria, CBS-related are recognized, based on the responsiveness to vitamin B_6 therapy. Vitamin B_6-responsive homocystinuria, CBS-related is usually milder than the vitamin B_6-non-responsive form. In both forms, thromboembolism is the major cause of early death and morbidity, and the risk is increased during and after pregnancies in females.[3]

Homocystinuria is included on all newborn screening panels in the United States[4]; however, not all individuals with homocystinuria will be identified via newborn screening.[3]

How is Homocystinuria, CBS-related inherited?

Homocystinuria, CBS-related is an autosomal recessive disease caused by mutations in the *CBS* gene. An individual who inherits one copy of a *CBS* gene mutation is a "carrier" and is not expected to have related health problems; however, they may be more likely to have low levels of vitamin B_{12} and folic acid.[1] An individual who inherits two mutations in this gene, one from each parent, is expected to be affected with homocystinuria, CBS-related.

If both members of a couple are carriers, the risk of having an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for Homocystinuria, CBS-related?

Homocystinuria, CBS-related can occur in individuals of all races and ethnicities, but it appears to be more common in Irish, German, Norwegian, and Qatari individuals[1]. The incidence in the United States is estimated to be 1 in 206,000, with an approximate carrier frequency of 1 in 227.[5]

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Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

- Screening, Technology and Research in Genetics: http://www.newbornscreening.info/Parents/aminoaciddisorders/CBS.html
- Children Living with Inherited Metabolic Diseases (CLIMB)**:** www.climb.org.uk

References

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