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. Individuals with homocystinuria have abnormalities in the enzyme cystathionine beta-synthase, which 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. Homocystinuria, CBS-related is also referred to as “classical homocystinuria”.

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:

- Developmental delays/intellectual disability
- 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 B₆. When started early in infancy, treatment may minimize or prevent intellectual disability and other complications of the disease. Some individuals are responsive to vitamin B₆ and their course of disease is usually milder than for those who are not responsive to vitamin B₆. Thromboembolism is the major cause of early death and morbidity, and the risk is increased during and after pregnancies in females.

Homocystinuria is included on all newborn screening panels in the United States; however, not all individuals with homocystinuria are identified by newborn screening.

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 B₁₂ and folic acid. An individual who inherits two CBS mutations, one from each parent, is expected to be affected with homocystinuria.

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. It appears to be more common in Irish, German, Norwegian, and Qatari individuals. The incidence in the United States is estimated to be 1 in 206,000, with an approximate carrier frequency of 1 in 227.

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.

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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