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My46 Trait Profile

Homocystinuria

Homocystinuria is a metabolic disorder caused by an inability to break down certain proteins. The most common form of homocystinuria is caused by mutations in the CBS gene which makes the protein called cystathionine beta-synthase.

Characteristics of Homocystinuria

Homocystinuria is a metabolic disorder caused by an inability to break down certain proteins. There are many forms of homocystinuria, however in the most common form, affected individuals are typically healthy at birth. For most, symptoms affecting the eyes, brain, blood, and bones often become present during early childhood. Almost all people with homocystinuria experience dislocation of the lens in their eye (i.e., ectopia lentis). Other less common eye problems include near-sightedness (i.e. myopia), progressive vision loss due to deterioration of the nerve that connects the eye to the brain (i.e., optic atrophy), cataracts, and separation of the retina in the eye (i.e., retinal detachment). Most individuals with homocystinuria have developmental delays (e.g., delays in speech, language, motor, social, or thinking skills) and/or intellectual disability. Adults with homocystinuria have an increased chance for developing mental health issues such as schizophrenia and depression. Homocystinuria also causes a significantly increased chance of abnormal blood clots, including stroke (blood clot in the brain). These blood clots may occur at any age. Tall stature and long limbs are characteristic of homocystinuria, as are abnormalities of the spine and rib cage. Osteoporosis is sometimes present and can be severe. The signs and symptoms seen in individuals with homocystinuria are highly variable.

Diagnosis/Testing

The most common form of homocystinuria is due to changes or mutations in a gene called CBS. This gene makes an enzyme called cystathionine beta-synthase. This enzyme is responsible for converting a molecule called homocysteine into another molecule called cystathionine. Mutations in the CBS gene decrease the amount of the enzyme in the body, and impair this conversion. The diagnosis of homocystinuria can be confirmed by measuring the level of CBS enzyme activity or by genetic testing of the CBS gene to see if mutations are present.

In the United States and in many other countries, babies are tested for homocystinuria at birth as part of mandatory newborn screening. Newborn screening is performed on a spot of the newborn’s blood that is taken by pricking the heel. This allows the diagnosis to be made in infancy so that treatment can be initiated early and many of the above symptoms can be prevented. The diagnosis of homocystinuria can also be made by a blood or urine test to detect the amount of homocysteine present. Homocysteine is a natural chemical which is present in everyone. People with homocystinuria have significantly increased levels of homocystine in both their blood and urine. The high level of homocystine is harmful to the body and causes the associated symptoms.

Management/Surveillance

The goal of treatment in homocystinuria is to keep the levels of homocysteine in the blood low in order to prevent symptoms. A low-protein diet is the primary form of treatment. Three vitamins: B12, folate, and betaine, are often recommended to help with homocysteine metabolism.

Some individuals with homocystinuria are said to be “B6-responsive.” This means that the level of homocysteine in their blood decreases if they take vitamin B6, also called pyridoxine. For these individuals, vitamin B6 therapy can

prevent or improve symptoms.

Women with homocystinuria are at increased risk to have an abnormal blood clot during and right after pregnancy. Pregnant women with homocystinuruia are often prescribed medication during their third trimester and after birth to decrease this risk.

Mode of inheritance

Homocystinuria caused by CBS deficiency is inherited in an autosomal recessive pattern. This means that an individual has to inherit two CBS mutations (i.e., one from each parent) to be affected with homocystinuria. If both parents are carriers of a CBS mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with homocystinuria. Babies born in the United States are screened for homocystinuria by newborn screening.

Risk to family members

Parents of a child with homocystinuria caused by CBS deficiency are carriers of homocystinuria. If a sibling of a child with homocystinuria is unaffected, he/she has a 2 in 3 (or 66%) chance of being a carrier of homocystinuria.

Special considerations

None

Resources

National Organization for Rare Disorders: Homocystinuria due to cystathionine beta-synthase deficiency
http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/463/viewFullReport
Genetics Home Reference: Homocystinuria
http://ghr.nlm.nih.gov/condition=homocystinuria
Medical Home Portal: Homocystinuria
http://www.medicalhomeportal.org/newborn/homocystinuria

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Schiff, M. et al. (2012)."Treatment of Inherited Homocystinurias." Neuropediatrics 43(6): 295-304.
The National Organization for Rare Disorders"Physcian's Guide to The Homocystinurias"

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