Homocystinuria

Homocystinuria is an inherited disorder in which the body is unable to properly break down certain building blocks of proteins (called amino acids) from ingested food. There are multiple forms of homocystinuria, which are distinguished by their signs and symptoms and genetic cause. The classical form of homocystinuria is due to a mutation in the CBS gene, which produces an enzyme called cystathionine beta-synthase. This enzyme is an important step in the pathway of breaking down the amino acids methionine and homocysteine to produce other amino acids. (Homocystinuria can also be caused by rare mutations in several other genes, preventing other enzymes in this pathway from functioning properly.) As a result of these mutations, methionine, homocysteine, and toxic byproducts build up in the blood and urine and interfere with the cross-linking of collagen fibers.

Newborn infants with homocystinuria usually appear healthy. Symptoms typically develop within the first year of life, although some people with a mild form of the disease may not develop features until later in childhood or adulthood. The first mild signs are often delayed development or failure to thrive, as well as increasing visual problems. As the child grows, physical deformities become more evident, such as a peaked or hollowed chest, scoliosis, high arches of the feet, fine brittle hair, a high palate with crowded teeth, knock knees, and long thin limbs and fingers.

The most common form of homocystinuria causes mental retardation, nearsightedness, dislocation of the lens of the eye, and brittle bones that are prone to breaking. Other less common forms of homocystinuria can cause more severe failure to thrive and developmental delay, seizures, movement disorders, and anemia. Serious complications of the disease include increased blood clotting, strokes, heart disease and heart attacks.

Inheritance

Classical homocystinuria is an autosomal recessive disease. To manifest the disease you need to have two faulty copies of gene and both of copy is not working. Person who carries one faulty copy of the gene won't manifest the disease because the normal copy of the gene will take over. If both parents are carrying the faulty gene the chance of their offspring to have the disease is one in four.

Diagnosis and Management

If a child is suspected to have homocystinuria, there are many tests that can be used to confirm the diagnosis, including screening for abnormally high levels of methionine and homocysteine in the blood and urine, genetic testing, x-rays to detect osteoporosis, and an eye exam to check for a dislocated lens. Genetic testing may additionally be helpful to identify carriers in the family and for either prenatal or neonatal screening for children at high risk of developing the disease.

Effective treatment for homocystinuria requires early diagnosis and initiation of therapy. No known treatment will reverse existing intellectual disability, but if the diagnosis is made while a patient is young, it can prevent many complications of the disease.

Although no cure exists for homocystinuria, there are multiple options for lessening the effects of this disease. Lifelong vitamin B6 supplements (also called pyridoxine) can help prevent mental retardation and behavior problems in about half of people affected

by the condition. Those who do not respond to B6 will need to eat a lifelong low-methionine diet. No meat, fish, dairy, or eggs are allowed, and flour, beans, and nuts must be restricted. Special low-methionine flours, breads, and pastas are often eaten, as well as a high-protein methionine-free formula. In addition, many patients with homocystinuria benefit from supplements such as betaine, folic acid, and vitamin B12. Children with this disorder should have regular blood and urine tests to check amino acid levels and modify their diet if necessary. With lifelong treatment, many children have normal growth and intelligence with a lower chance of blood clots, heart disease, eye problems, and seizures.

Homocystinuria in Arab Populations

Homocystinuria is overall a very rare disorder, affecting only about 1 in every 200,000 to 335,000 live births worldwide. Where data is available, disease frequency in the Middle East seems to be higher than these worldwide figures: reported incidence in Oman is 1 in approximately 128,200 births, and cases have also been documented in Bahrain and Saudi Arabia. The highest incidence of homocystinuria in the world is found in Qatar, where 1 in 1,800 babies are affected. Because of this very high rate, accurate neonatal genetic testing in Qatari populations is crucial to detect and treat affected children before they can suffer developmental delays or mental retardation.

Homocystinuria

A recent study has suggested that the Paharaoh Akhenaten might have suffered from homocystinuria. This suggestion is based on ancient images of the Pharaoh, which depict him with skeletal abnormalities and a long thin face. From their images, his parents seem to be unaffected, while his wife Nefrititi and all six of their daughters are affected. His minor wife and their son, Tutankhamen, on the other hand appear normal. Taking these images as being honest depictions rather than artistic interpretations, a pattern of autosomal recessive inheritance emerges. It is likely that the Pharaoh suffered from homocystinuria. He died at 33-years of age, and it is possible that this was due to thromboembolism.