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My46 Trait Profile

Primary carnitine deficiency

Other Names: Carnitine uptake deficiency, Systemic primary carnitine deficiency

Primary carnitine deficiency is a genetic disorder in which the body is unable to use certain fats as a source of energy when not eating. It is caused by mutations in the SLC22A5 gene that make a protein called solute carrier family 22 member 5.

Characteristics of Primary carnitine deficiency

Primary carnitine deficiency (PCD) is a genetic disorder in which the body is unable to use certain fats as a source of energy when fasting (not eating). Individuals with PCD are unable to make a specific protein called solute carrier family 22 member 5, which is used to transport a substance called carnitine in and out of cells. Carnitine is a natural substance that is taken in through foods like meats and dairy (milk, butter, etc.). Carnitine plays a role in a process called fatty acid oxidation (FAO). When energy sources such as sugar become low, the body breaks down fatty acids as a source for energy. FAO occurs in a part of the cell called the mitochondria. Carnitine moves fatty acids to the mitochondria where they can be used for energy.

Symptoms of PCD can vary widely in terms of severity and onset. Typically, symptoms of PCD are triggered when a person is unable or unwilling to eat, such as during an illness. About half of individuals with PCD will present in infancy (between 3 months to 2 years) with episodes of low blood sugar (hypoglycemia), vomiting, lethargy, irritability, poor feeding, possible brain damage (encephalopathy), and an enlarged heart (cardiomyopathy). Death from coma or cardiac failure may occur without proper treatment. The remaining half of individuals present in later childhood (after age four) with fatigue, muscle weakness, and cardiomyopathy. Some people have no symptoms and may only find out they have the condition by chance. Regardless of onset or severity, all people are at risk for heart and liver problems, as well as coma and sudden death.

The prognosis is very good for individuals who receive early treatment. They typically have normal intelligence and development, and few chronic health problems. The major health concern for individuals with PCD is sudden death due to an irregular heartbeat (cardiac arrhythmias), especially if they are not receiving treatment.

Diagnosis/Testing

Most individuals with PCD have changes or mutations in the SLC22A5 gene. This gene makes a protein called solute carrier family 22 member 5 that is responsible for delivering carnitine in and out of cells. Mutations in this gene cause the protein to be made incorrectly which means carnitine is unable to enter the cell. This leads to a lack of carnitine. Without carnitine, fatty acids cannot get into the mitochondria to be broken down and the body cannot get the energy it needs. In addition, fatty acids cannot exit the cell, which can cause a buildup, affecting the liver, heart and muscles. These two issues explain the symptoms seen with PCD.

Testing in the SLC22A5 gene is often done to confirm a diagnosis of PCD. If this testing does not find a mutation, then a skin biopsy may be done to study the uptake of carnitine by the cells.

Many babies with PCD are diagnosed early in life through newborn screening (NBS). NBS tests a spot of blood from the baby’s heel. A child with PCD will have a low amount of carnitine. Sometimes, asymptomatic women (women who do not show signs of the condition) are diagnosed with PCD after having a child. Newborn infants get all of their

carnitine from their mother. The newborn of a mother with PCD will therefore have low carnitine levels at birth and may falsely test positive for PCD. When a newborn screen is positive for PCD, the mother is evaluated for low carnitine levels to determine if she has PCD.

Management/Surveillance

The primary treatment for PCD is carnitine supplementation (carnitine is added to an individual's diet). A high dose of carnitine will help stabilize carnitine levels, although they may never reach a normal range. This supplementation can help prevent irreversible organ damage and improve muscle and heart function. The dose of carnitine is monitored and adjusted with blood testing to ensure it is at the appropriate level. Long-term studies have shown that appropriate treatment with carnitine completely reverses the cardiomyopathy. In addition, patients on therapy report normal muscle tone.

Individuals with PCD should be followed by a cardiologist in order to evaluate their risk of cardiac arrhythmias. Individuals with PCD are followed by a metabolic geneticist.

Mode of inheritance

PCD is inherited in an autosomal recessive pattern. This means that an individual has to inherit two SLC22A5 mutations (i.e., one from each parent) to be affected with PCD. If both parents are carriers of a SLC22A5 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with PCD. Babies born in the United States are screened for PCD by newborn screening.

Risk to family members

Parents of a child with PCD are carriers of PCD. If a sibling of a child with PCD is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of PCD.

Special considerations

PCD may be exacerbated during pregnancy when energy needs increase.

Resources

Children Living with Inherited Metabolic Diseases (CLIMB)
http://www.climb.org.uk
FOD Family Support Group (Fatty Oxidation Disorder) Genetics Home Reference: Primary Carnitine Deficiency
http://www.fodsupport.org
Genetics Home Reference: Primary Carnitine Deficiency
http://ghr.nlm.nih.gov/condition/primary-carnitine-deficiency
Medical Home Portal: Newborn Disorders, Carnitine Uptake Deficiency
http://www.medicalhomeportal.org/newborn/carnitine-uptake-deficiency

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