CUD: Carnitine Uptake Defect

Carnitine uptake defect (also known as systemic primary carnitine deficiency, carnitine transport defect, CUD or CDSP) is a type of genetic condition categorized as a fatty acid oxidation disorder (also known as a FAOD). The body usually gets its energy by breaking down, or burning, fats and sugars. People with FAODs cannot properly break down certain types of fats. In CUD, a small molecule called carnitine is not able to do its job of helping fats enter the mitochondria (our powerhouse cells) where they can be broken down to create energy. This prevents the body from creating enough energy during times of stress, illness, fasting, and exercise, which can lead to medical symptoms.

Alternative Names

- Systemic Primary Carnitine Deficiency
- CUD
- CDSP

Genetics

People usually have two copies of the SLC22A5 gene, one inherited from each parent. CUD occurs when there are changes in both copies of the SLC22A5 gene (autosomal recessive inheritance). Someone who has a change in only one copy of the SLC22A5 gene is called a carrier, and they usually do not have any medical symptoms. If both parents are carriers, there is a 1 in 4 chance with each pregnancy that their child will have CUD. Both males and females can have CUD.

Frequency

In the United States, CUD is rare and occurs in approximately 1 in every 100,000 newborns. In Japan, CUD is much more common and occurs in approximately 1 in every 40,000 newborns

Signs and Symptoms

CUD can cause a range of signs and symptoms. Whether your child was diagnosed via newborn screening may also affect when, if, and how these symptoms present. Always check with your doctor if your child is doing something out of "their" normal, as every child may present with symptoms a little differently.

CUD usually presents between the ages of three months to seven years after an episode of minor illness like a stomach virus or ear infection, but older children and adults can also be diagnosed. Signs and symptoms may include:

- Irritability
- Extreme tiredness (lethargy)
- Refusing to eat
- Weak muscles and poor muscle tone (hypotonia)
- Low blood sugar (hypoglycemia)
- Low ketones (hypoketotic)
- Enlarged, weakened heart (dilated cardiomyopathy)
- Liver damage

- Mildly high creatine kinase (sign of muscle damage)
- Gradual increase of muscle weakness
- Fat deposits in the muscle
- Intravenous (IV) sugar-containing fluids called D10 during metabolic crisis

In some cases, CUD can cause fetal hydrops, a dangerous form of fluid buildup in a baby that occurs before birth.

Diagnosis

Most cases of CUD are identified by routine newborn screening. If newborn screening is suggestive of CUD, additional tests may be performed including:

Repeat testing on cultured skin cells (fibroblasts) or white blood cells (lymphoblasts)
Genetic testing to look for changes in the SLC22A5 gene

In some cases, a diagnosis can be made before birth if there is a known family history of CUD or if a baby has fetal hydrops. This testing can be complicated because mothers provide carnitine to babies during pregnancy.

Routine newborn screening may not detect everyone with CUD. If blood for screening is taken too soon after birth, a baby may still have carnitine leftover from its mother. On the other hand, sometimes newborn screening shows a false positive if the mother has a mild form of CUD.

If there is a family history of CUD, or if parents are known carriers, prenatal testing can be performed on amniotic fluid (the fluid surrounding a baby) or chorionic villi (a specific part of the placenta).

Treatment and Management

Before beginning any treatment or therapy, please consult with your physician.

Treatment and management of CUD may include:

- L-carnitine supplements
- Routine management of heart conditions

Sometimes an L-carnitine supplement causes people with CUD to develop a fishy odor. This odor is harmless and can be reduced by adding a medicine called metronidazole to the treatment.

Parents should call their health care provider immediately if babies show symptoms like excessive sleepiness, vomiting, diarrhea, a fever, poor appetite, or an infection. Medical treatment should be sought immediately if there is loss of consciousness or severe confusion (decompensation), as these are signs of dangerously low blood sugar.

Patients should discuss the appropriate preparation for anesthesia with their metabolic team.
All patients should have an emergency protocol letter, written and signed by their doctor, that details their prescribed treatment during crisis and in emergency room settings, to manage severe episodes.

Clinical Trials

For specific details on other clinical trials, visit the MitoAction Clinical Trials page or www.clinicaltrials.gov.

Resources

- The National Institutes of Health: Primary carnitine deficiency - About the Disease
- The INFORM Network: CUD Deficiency | Fatty Acid Oxidation Disorders Diagnosis
- National Organization for Rare Disorders (NORD): Systemic Primary Carnitine Deficiency - NORD (National Organization for Rare Disorders)

Connecting with others who are impacted by a rare disease allows for important information to be shared about day-to day life, prevents isolation, and gives hope. Please contact MitoAction for peer support opportunities at 888-MITO-411 or email mito411@mitoaction.org. Other resources we recommend are:

- New Patient Kit for FAODs
- Planning and Preparation
- Monthly Expert Series
- Energy in Action Podcast

MitoAction does not provide medical advice, diagnosis, treatment, or legal advice. It is essential that all those living with or caring for someone with a Mitochondrial or FAOD disease have an emergency protocol letter. These letters, which are written and signed by a doctor, share details about prescribed treatment during crises and in emergency room settings. Always check with your doctor if you or your child has concerns as everyone may present with symptoms differently. Before beginning any treatment or therapy, please consult with your physician.