CARNITINE TRANSPORTER DEFICIENCY

Clinical Features
There are two forms of Carnitine Transporter Deficiency, one with neonatal onset between 3-30 months of age, and one with late onset which starts from 1-7 years of age. Fifty percent of patients develop multiple attacks of acute encephalopathy, with vomiting, confusion, and stupor progressing to coma between birth and 30 months of age. Infants display hypoketotic hypoglycemia, hyperammonemia, elevated liver functions, some with cardiomyopathy (generally dilated) and/or skeletal muscle weakness. A few patients who have not had documented episodes of hypoglycemia have presented with nonspecific developmental delay. Carnitine Transporter Deficiency may be a cause of sudden unexpected infant death. The other fifty percent present with progressive dilated cardiomegaly between 1-7 years of age. They have associated skeletal muscle weakness, but no evidence of hypoglycemia. Cognitive development is not impaired. Several patients have had anemia that did not respond to iron therapy. Others have had hepatomegaly, lipid deposits in muscle and/or liver steatosis.

This disorder is a true primary systemic carnitine deficiency for several reasons: It results in extremely low plasma and tissue carnitine levels; it is not secondary to a mitochondrial defect of organic acid oxidation; and patients with this disorder respond dramatically to carnitine therapy. Levels of plasma carnitine in affected patients fall to near zero within a few days of stopping carnitine supplementation. During this time, carnitine excretion in the urine remains high, even at low plasma levels. Failure to reabsorb carnitine in the kidney results in very low plasma carnitine levels, which, in turn, diminish the hepatic uptake of carnitine by passive diffusion. Hence, ketogenesis is impaired, but is restored to normal on carnitine supplementation.

Diagnosis
Newborn screening—Tandem mass spectrometry-C0-free carnitine-very low; all carnitine values low. Confirmation—a second sample may be requested or follow up testing will be done at the Metabolic Treatment Center at Yale or UCONN Genetics.

Monitoring
Clinical observation is the most important tool for monitoring patients with this disorder. They should be observed for recurrent vomiting, refusal to eat, increased lethargy, apnea or seizures. In these situations, immediate evaluation in the emergency room is necessary. In situations of metabolic decompensation hypoglycemia can develop, but a normal blood glucose does not rule out metabolic instability and should never be a reason to delay therapy. It is also important for the primary care provider and the Metabolic Treatment Center to develop an on-going collaborative relationship in caring for these patients.

Treatment
- Avoid fasting.
- Feed at regular intervals during the day and limit overnight fasting.
- Should not go without food intake longer than 4 hours for the first 4 months of life; 6 hours for ages 4-8 months; and no longer than 8 hours thereafter.
- Supplementation with L-carnitine restores plasma carnitine levels to nearly normal.
- The use of cornstarch therapy is an ongoing treatment and is even more necessary during acute illness.
- If the child is vomiting or refuses to eat, (s)he needs to be taken to an emergency room for IV administration of 10% dextrose.

1/19/2005
The parents usually have an emergency protocol with them. This protocol, provided by the Metabolic Treatment Center, contains basic information about the disorder, necessary diagnostic investigations and guidelines for treatment.

Infants and children with Carnitine Transporter Deficiency should have regularly scheduled visits at the Metabolic Treatment Center.

**Illness**
- Any illness can potentially lead to metabolic decompensation
- Prevention and/or early intervention is of particular importance
- Provide high-carbohydrate feedings including cornstarch
- Avoid dehydration
- Closely monitor blood glucose and intake; even if blood glucose is normal, metabolic decompensation can occur.
- Consult with the Metabolic Treatment Center within 24 hours of the onset of the illness

**Immunization**
- Immunizations must be kept current.
- All children with Carnitine Transporter Deficiency should have a yearly vaccine for influenza.
- There is no contraindication to any immunization because of Carnitine Transporter Deficiency.
- Parents and physicians should be alerted to the need for immediate evaluation if high fever, lethargy or vomiting occurs in the first 24 hours.
- After an immunization without any other clinical symptoms, administration of acetaminophen or ibuprofen is warranted.

**Surgical/surgical procedures**
- Discuss any plans for surgical and dental procedures with the Metabolic Treatment Center
- Infants and children with Carnitine Transporter Deficiency can undergo necessary anesthetic/surgical procedures.
- Any surgical procedure constitutes a potentially catabolic situation.
- Any surgery should include hospitalization pre- and postoperatively.
- Preoperative fasting should be avoided with 10% dextrose being started preoperatively and continuing postoperatively until the child is eating and drinking well.
- If complicated surgery, or a postoperative period, as an inpatient is required, the procedure should be done at a hospital with a metabolic service.

**Growth and development**
- It is crucial to closely monitor all growth parameters on a regular basis.
- In cases with neurological deficits, the child should be referred to an early intervention program and developmental progress closely monitored by both the metabolic team and the primary care provider.

The information provided is offered for general informational and educational purposes only. It is not offered as and does not constitute medical advice. In no way are any of the materials presented meant to be a substitute for professional medical care or attention by a qualified practitioner, nor should they be construed as such. Contact your physician if there are any concerns or questions.

1/19/2005