



State of CT
Genetics Newborn Screening Program
Health Care Provider Fact Sheet

Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD)

Introduction

Very long-chain acyl-CoA Dehydrogenase Deficiency (VLCADD) is an autosomal recessive disorder of fatty acid oxidation resulting in an inability to breakdown long-chain fatty acids for ketone and ATP synthesis (see figure). Clinical symptoms are often triggered by prolonged fasting, infection or exercise. VLCADD is treated with diet and supplemental carnitine.

The normal physiology begins with reduced glucose intake as a result of a prolonged fasting state or increased energy needs from a catabolic state (infection, stress, etc.) not sufficiently provided for by caloric intake. The resulting hypoglycemia leads to mobilization of free fatty acids (FFAs) which enter the mitochondria via the carnitine cycle. In the mitochondria, as shown in the diagram above, the fatty acids in the acyl Co-A form are normally oxidized to acetyl-CoA which is used to produce the ketones that can supply the energy needs to compensate for the lack of adequate glucose. However, a deficiency of VLCAD prevents ketone formation. The block at VLCAD also results in the accumulation of fatty acid intermediates that inhibit gluconeogenesis (thus preventing endogenous glucose production), and produces a toxic effect on the liver leading to metabolic acidosis. Muscle, particularly myocardium, requires a continuous energy source, and, in its absence, leads to lethargy, hypotonia and hypertrophic cardiomyopathy.

Clinical Features

- Hypertrophic cardiomyopathy
- Lethargy
- Hypoketotic Hypoglycemia
- Seizures
- Hepatic encephalopathy
- Coma
- Sudden death

The initial presentation may occur in the neonatal period, but more often when the infant is being weaned from night time feeds. The usual picture is nausea, vomiting and/or lethargy after a period of fasting. This can progress to hypoglycemic seizures or coma within 1-2 hours of ONSET of symptoms. There may, or may not, be a history of a recent viral infection associated with diminished oral intake, or of a similar episode in the past. Fatty acid oxidation disorders (FAODs) are responsible for a small but significant proportion of sudden infant death syndrome which may be preventable with prompt recognition and treatment.

Approximately 50% of episodes present as infants with nonketotic hypoglycemia, hepatic dysfunction and cardiomyopathy, and this has been generally lethal.

33% present in late infancy or childhood with episodes of nonketotic hypoglycemia and hepatic dysfunction, but no cardiac involvement.

There is generally a mild hyperammonemia, with increased lactate, and creatine kinase.

Approximately 20% present as adolescents or adults with symptoms limited to muscle fatigue, rhabdomyolysis and myoglobinuria triggered by exercise or fasting. There is no hypoglycemia or cardiac involvement.

NOTE that in the acute crises patients can be seriously ill WITHOUT hypoglycemia although typically FAOD crises are associated with hypoglycemia. At these times the urine typically tests 'absent' or 'small' for the presence of ketones. Liver function tests may be mildly elevated; hyperammonemia and hyperuricemia are often present during acute episodes.

Diagnosis

Newborn screening—Tandem mass spectrometry identifies elevations in plasma long-chain acylcarnitines (C14:1- elevated, C16- elevated, C18:1- elevated)

Confirmation— a second sample may be requested or follow up testing will be done at the Metabolic Treatment Center at Yale or UCONN Genetics.

Situations that risk metabolic decompensation

Children with VLCADD may be clinically asymptomatic. Metabolic decompensation can be triggered by the catabolic processes that occur in the course of an infection, post-immunization or with a prolonged period of fasting. Lethargy, vomiting, tachypnea or apnea, with or without hypoglycemia, are typical clinical features. During acute illnesses or periods of poor oral intake a regular feeding schedule is particularly important, as often as every four hours around the clock. 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. The parents usually have an emergency protocol with them, which contains basic information about the disorder, necessary diagnostic investigations and guidelines for treatment.

Monitoring

Clinical observation is the most important tool for monitoring patients with VLCADD. They should be observed for lethargy, recurrent vomiting, refusal to eat, tachypnea or apnea. In these situations immediate evaluation in the ER is necessary. In situations of metabolic decompensation hypoglycemia with little or no urinary ketones can develop, but a normal blood glucose level does not rule out metabolic instability and should never be a reason to delay therapy.

Cardiac evaluation

Any child diagnosed with VLCADD should be evaluated by a pediatric cardiologist for the presence of cardiomyopathy upon diagnosis, followed by, at least, yearly evaluations. Clinical symptoms suggesting cardiomyopathy are tachypnea, hepatomegaly, tachycardia, feeding problems and exercise intolerance, but cardiomyopathy can be present without any clinical symptoms.

Treatment

- Avoid fasting and prolonged exercise.
- 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
- The Metabolic Treatment Center will set a patient's diet prescription that determines the optimum percentage of fat, carbohydrate, and protein.
- Restrict very long chain fatty acids to 10% of total energy
- Carnitine supplements—monitor and add carnitines only if necessary; There are concerns that long chain acylcarnitines may induce arrhythmias.
- Supplementation with Medium Chain Triglycerides Oil (MCT) provides 10-20% of total energy.
- Increased carbohydrate intake and cornstarch therapy is necessary during acute illness. 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 at least 10% dextrose. These patients may go on to develop metabolic acidosis or hyperammonemia, in addition to severe hypoglycemia.
- The parents should have an emergency protocol with them at all times. This protocol, provided by the Metabolic Treatment Center, contains basic information about the disorder, necessary diagnostic investigations and guidelines for treatment.
- Cardiac and ophthalmologic status should be reviewed on a regular basis.
- Infants and children with VLCADD should have regularly scheduled visits at the Metabolic Treatment Center.
- VLCADD chronic management is complicated as many children take a significant amount of time (days to weeks) to improve clinically even once their biochemical parameters have normalized. Particular problems include gradual improvement in mental status, hypotonia, hepatomegaly and cardiomyopathy. It is important to be aware that despite therapy children with VLCADD have died or been left with chronic neurologic, cardiac and hepatic problems.

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 VLCADD should have a yearly vaccine for influenza.
- There is no contraindication to any immunization because of VLCADD.
- 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.

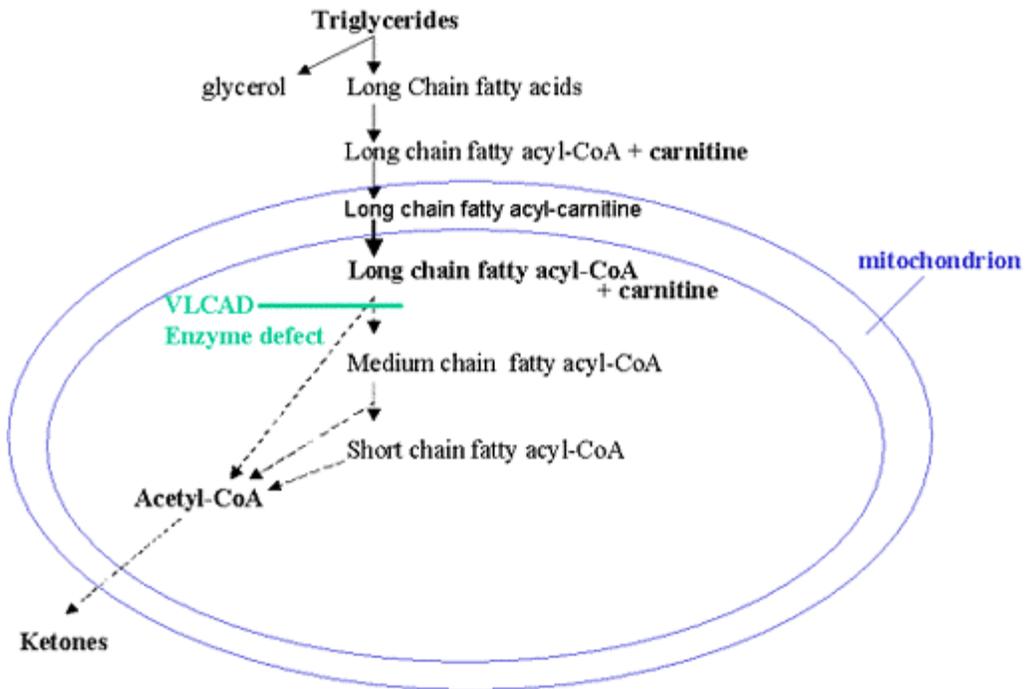
Surgical/surgical procedures

- Discuss any plans for surgical and dental procedures with the Metabolic Treatment Center
- Infants and children with VLCADD 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.

Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD)



860-509-8081

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.