

PROTOCOL FOR NEWBORN SCREENING RESULT

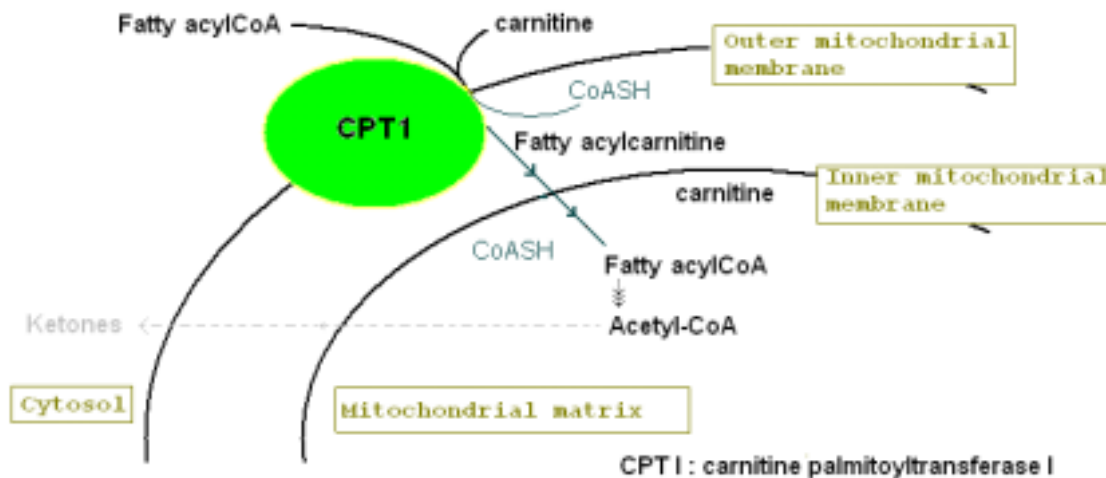
Elevated acylcarnitine, associated with Carnitine Palmitoyltransferase I (CPT I) Deficiency

First Newborn screening result

markedly elevated carnitine profile. Probable CPT I deficiency

markedly elevated carnitine profile. Probable CPT I deficiency

Carnitine palmitoyltransferase I (CPT I deficiency) is an enzyme that catalyzes the binding of fatty acids to carnitine, forming the fatty acylcarnitines that allow the transport of fatty acids into mitochondria where they are oxidized and thus utilized for energy. In CPT I deficiency the lack of binding to carnitine excludes the fatty acids from the mitochondria. Consequently there is decreased tolerance for fasting or any hypoglycemia state wherein energy must be supplied from fats. Death during a metabolic crisis can ensue.



History and examination

The infant and parent(s) must be seen within the next day or two following notification from the newborn screening laboratory. A METABOLIC PHYSICIAN MUST BE CONSULTED.

History

For CPT I deficiency the infant may have a normal history. On occasion however, there is a history of neonatal lethargy, acute liver failure, seizures or coma. Since both these conditions are autosomal recessive genetic disorders, there is a 25% chance that sibs of the identified infant may also have CPT I deficiency. A family history of siblings or other children becoming seriously ill particularly with liver failure or sudden death is very significant as is a history of the child's mother having the HELLP syndrome during pregnancy (hemolysis, elevated liver enzymes and low platelets) or acute fatty liver of pregnancy (AFLP).

Examination

The infant may be entirely well. Neonatal signs include seizures, hepatomegaly and, rarely, arrhythmias and mild cardiomegaly. Laboratory findings during neonatal illness include hypoglycemia, metabolic acidosis, hyperammonemia, elevated CK and markedly increased carnitine. ANY signs of illness must be treated as a medical emergency and treated immediately by a metabolic physician.

If the child appears well it is still essential to refer to the metabolic center to ensure that the child and family receive the necessary treatment and guidance to prevent any morbidity.

Contact the metabolic physician for markedly elevated carnitine profile

ENSURE THAT THE REPEAT NEWBORN SCREENING SAMPLE IS SENT TO THE NEWBORN SCREENING LABORATORY AND THE RESULT OBTAINED ASAP (Go to **NNSGRC** for the state labs)

Discussion with parents for markedly elevated carnitine profile

Contact metabolic physician for markedly elevated carnitine profile

Your local metabolic physician can be found via [metabolic physicians and specialists](#)

The metabolic physician's role

- Provides you with information on CPT I deficiency .
- Discusses, in further detail, the meaning of the test result with the family
- Starts appropriate [treatment](#)
- Provides supportive counseling for the family
- Undertakes [definitive investigations](#)
- Provides genetic / prenatal counseling
- Hospitalizes, if necessary, in a metabolic unit for acute illnesses. These infants cannot be managed conservatively when they become ill. The threshold should be very low for intravenous 10% dextrose and very close metabolic monitoring by a metabolic physician.

Return to [discussion with parents for markedly elevated carnitine profile](#)

Discussion with parents for markedly elevated carnitine profile

Response to a reported newborn screening result must be undertaken in two parts;

1. Initial contact with the family, often by phone, to inform them of the newborn screening result
2. Meeting with the family at the office.

Initial communication,

Many parents want to know what the result is testing positive for and are reassured if their doctor has knowledge of CPT I deficiency or has taken the time to find out about the condition when informing the family (see **commonly asked questions**).

A highly elevated carnitine level (of $> 75 \mu\text{mol/L}$ (and a free carnitine/ [C16+C18] ratio > 175) probably means that the infant has CPT I deficiency. CPT I deficiency is a disease in which fat cannot be properly utilized for energy. Treatment can help. However, if not treated preventatively, children can become ill very rapidly if their blood sugar drops too low and death can occur. The mainstay of treatment is prevention. It is essential that parents arrange to see a metabolic doctor as soon as possible.

In the office

Many parents do not understand newborn screening or the need to treat their apparently healthy baby.

Parental anxiety will be high and it is important to reassure them that

- Treatment is available.
- But note that failure to treat a baby with CPT I deficiency may result in life threatening illness, neurological sequelae or death.

Treatment for CPT I deficiency is based on ensuring that hypoglycemia through fasting or the increased energy requirement of the body when sick is avoided. Therefore, when well the baby should initially be fed every 4 hours around the clock. If the infant becomes ill, supplemental glucose as 10% dextrose given intravenously is often required to maintain energy levels and avoid life threatening energy deficit. When this happens, the metabolic doctor must be contacted and involved to ensure that all the necessary metabolic tests and measures are carried out.

Further counseling, treatment and a more detailed assessment and testing of the infant is required; therefore

contact metabolic physician for markedly elevated carnitine profile

Commonly asked questions for CPT I deficiency

1. What is CPT I deficiency?

CPT I deficiency, also known as carnitine palmitoyltransferase I deficiency, is a fatty acid oxidation disorder (FAOD). It is a defect in one of the enzymes involved in the deployment of fats to fuel that can be used by the body. It becomes very important when the body is low on glucose or needs additional fuel such as when the child has not eaten for a period of time, during infections and other illnesses, during operations and when exercising vigorously.

2. How and when will we know if my baby has CPT I deficiency?

If your baby's newborn screening result showed a high free carnitine and an elevated carnitine ratio he or she probably has CPT I deficiency. If the ratio was between 100-175 your baby either could still have CPT I deficiency or the result may have been false positive. The newborn screening test will be repeated and additional tests will be undertaken to help determine if your baby has CPT I deficiency or not. Typically the results of these tests take up to 4 days to come back. Depending on the test results, additional testing can take a variable amount of time to confirm the diagnosis. In a very small minority of cases, it can be difficult to determine whether a child is affected or not.

3. How did my baby get this?

CPT I deficiency is an autosomal recessive disorder. This means that your baby has two mutated CPT1 genes, one from the mother and one from the father. Having only one mutated CPT I gene (a carrier) does not affect a person at all.

4. What does it mean for my child?

If your baby has CPT I deficiency, he or she will have to be fed regularly on a carbohydrate rich fat modified/decreased diet and can not be allowed to miss a meal. Medium chain triglyceride supplementation provides fat energy past the enzyme block. Carnitine should not be provided as, unlike all the other fatty acid oxidation defects, carnitine is elevated in CPT I deficiency. If he or she becomes ill, it may well be necessary early in the illness (i.e. when it might be considered mild) to provide extra energy in the form of glucose through addition to food or, if necessary, by intravenous drip.

5. What is the treatment? Does it work? Is the diet difficult to do/expensive?

CPT I deficiency is primarily treated by a high carbohydrate and fat modified/decreased diet that is given at regular defined intervals around the clock. As the diet is essentially normal it should not be a financial burden. However, ensuring that you and the baby wake up, initially every 4 hours, can be physically exhausting over time. If possible you should anticipate this and try and ensure that you have support from your spouse or other close contacts to assist you so that you may enjoy your time with your baby.

6. What about my other children/future children?

As CPT I deficiency is an inherited condition it is essential to have your other children tested. Children from the same father and mother as the affected infant have a 1 in 4 (25%) chance of having CPT I deficiency. Your other children can appear healthy and still have CPT I deficiency. If they have CPT I deficiency, successfully having weathered illnesses in the past is no guarantee that an illness in the future will not have serious consequences.

Since there is a risk for having a future child with CPT I deficiency it is important to let your obstetrician and pediatrician know that you have a child with CPT I deficiency if you are planning future pregnancies so that they may discuss the options with you and prepare accordingly. The obstetrician should furthermore be alerted to the association between CPT I deficiency and the HELLP and AFLP syndromes to the mother during pregnancy (see "History and Examination section" above).

Definitive Investigations

1. Quantitative urine organic acids

In symptomatic patients standard urine organic acid profiles may show a mild dicarboxylic aciduria but can also be uninformative

2. Plasma acylcarnitines

The profile of patients with CPT I deficiency is characterized by elevated plasma carnitine (essentially all of which is free carnitine) and low levels of the acylcarnitines.

3. Acute illness labs

Hypoketotic hypoglycemia at all ages, is suggestive of a fatty acid oxidation disorder CK and liver function tests should be assayed as well as free and total carnitine.

The lab tests may not be informative when the infant is well, therefore these tests are most valuable at times of acute illness. Labs ideally obtained for diagnostic purposes during acute illness in order of priority include plasma glucose, urinalysis, plasma free and total carnitine and acylcarnitines, plasma amino acids and urine for organic acids. However, treatment should **NEVER** be delayed to obtain these labs and acute management labs should take priority .

4. Enzyme assay

CPT I enzyme activity, though pathologically hepatospecific, can be measured in cultured fibroblast cells. Levels in infantile/neonatal variants of CPT I are typically 5-20% of control values [Go to genetests.](#)

5. Molecular testing

Mutation testing of the gene soon may be helpful but molecular testing is not routinely available yet.

Treatment

Diet

The mainstay in the treatment of CPT I deficiency is avoidance of fasting. Infants require frequent feedings, initially every 4 hours. A relatively high carbohydrate modified fat diet is helpful. Medium chain triglyceride (MCT) oil is helpful. BUT, MCT oil should only be initiated by the metabolic physician following comprehensive workup as it will worsen several other fatty acid oxidation defects.

Carnitine

Carnitine is contraindicated.

Acute illness treatment

Any time the child is sick an evaluation should be made and the child's metabolic physician contacted. Prophylactic intravenous 10% glucose should be given if the child is unable to eat, vomiting or physiologically stressed, even mildly. The threshold for aggressive treatment should be very low.

All patients should be provided with an up to date personalized "emergency" letter to give to ER, or other doctors, who are probably not familiar with CPT I deficiency. This letter should include management issues and emphasize the importance of preventive measures (*e.g.*, IV 10% glucose regardless of "normal" laboratory results and the telephone numbers of the patient's metabolic specialist who needs to be contacted to discuss management).