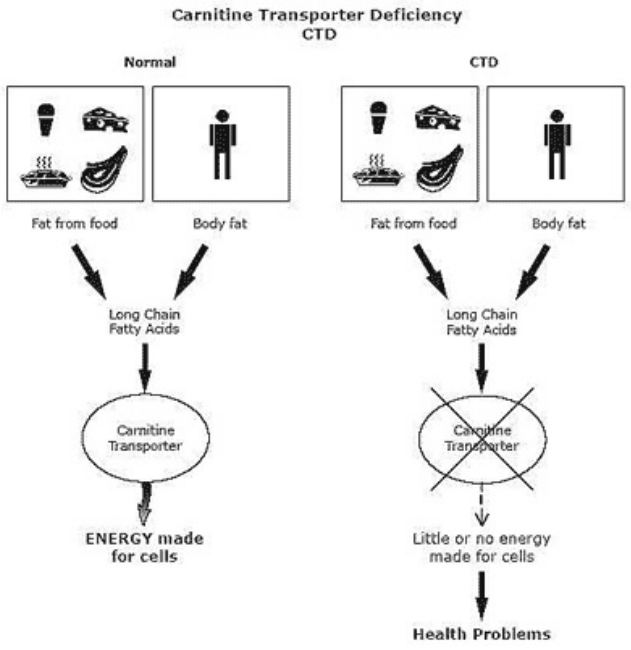
CARNITINE TRANSPORTER DEFICIENCY (CTD) OR CARNITINE UPTAKE DISORDER (CUD)
A fact sheet for parents/carers

What is Carnitine transporter deficiency (CTD)?

CTD stands for "carnitine transporter deficiency". It is one type of fatty acid oxidation disorder. People with CTD have problems using fat as energy for the body.

What causes Carnitine transporter deficiency (CTD)?



CTD occurs when an enzyme, called "carnitine transporter" (CT), is either missing or not working properly. This enzyme's job is to carry a substance called carnitine into our cells. Carnitine helps the body make energy from the fat in food. It also helps us use fat already stored in the body.

Energy from fat keeps us going whenever our bodies run low of their main source of energy, a type of sugar called glucose. Our bodies rely on fat when we don't eat for a stretch of time – like when we miss a meal or when we sleep.

When the normal CT enzyme is missing or not working well, the body cannot use fat for energy. Instead, it must rely solely on glucose. Although glucose is a good source of energy, there is a limited amount available. Once the glucose has been used up, the body tries to use fat without success. This leads to low blood sugar, called hypoglycemia, and to the build up of harmful substances in the blood.

If Carnitine transporter deficiency (CTD) is not treated, what problems occur?

There are two main forms of CTD: one begins in infancy, the other in childhood.

CTD in infants: Babies with CTD first show symptoms between birth and age three. CTD can cause bouts of illness called metabolic crisis. Some of the first symptoms of a metabolic crisis are:

- extreme sleepiness
- behavior changes
- irritable mood

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- poor appetite

Other symptoms then follow:

- fever
- nausea
- diarrhea
- vomiting
- hypoglycemia

If a metabolic crisis is not treated, a child with CTD can develop:

- breathing problems
- swelling of the brain
- seizures
- coma, sometimes leading to death

Babies who are not treated may have other effects:

- enlarged heart
- enlarged liver
- muscle weakness
- anemia

Repeated episodes of metabolic crisis can cause brain damage. This can result in learning problems or mental retardation. Symptoms of a metabolic crisis often happen after having nothing to eat for more than a few hours. Symptoms are also more likely when a child with CTD gets sick or has an infection.

CTD in children: Children with CTD appear perfectly normal until symptoms begin, usually between the ages of one and seven. Some of the effects of childhood CTD are:

- enlarged heart
- muscle weakness
- if left untreated, risk of heart failure and death

Children with this type of CTD do not have episodes of hypoglycemia or metabolic crises. Their intelligence is not affected. Some children with CTD deficiency never have symptoms and are only found to be affected after a brother or sister is diagnosed.

What is the treatment for Carnitine transporter deficiency (CTD)?

Your baby's primary doctor will work with a metabolic doctor to care for your child. Your doctor may also suggest that you meet with a dietician familiar with CTD. Certain treatments may be advised for some children but not others. When necessary, treatment is usually needed throughout life. The following are treatments often recommended for children with CTD:

1. L-carnitine

The main treatment for CTD is lifelong use of L-carnitine. This is a safe and natural substance

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that helps body cells make energy. It also helps the body get rid of harmful wastes. L-carnitine can reverse the heart problems and muscle weakness that happen in children with CTD. Your doctor will decide whether or not your child needs L-carnitine. Unless you are advised otherwise, use only L-carnitine prescribed by your doctor. Do not use L-carnitine without checking with your doctor.

2. Avoid going a long time without food

Infants and young children with CTD need to eat frequently to prevent a metabolic crisis. Your metabolic doctor will tell you how often your child needs to be fed. In general, it is often suggested that infants be fed every four to six hours. Some babies need to eat even more frequently than this. It is important that infants be fed during the night. They may need to be woken up to eat if they do not wake up on their own. Your metabolic doctor and dietician will give you an appropriate feeding plan for your infant. Your doctor will also give you a 'sick day' plan tailored to your child's needs for you to follow during illnesses or other times when your child will not eat.

Your metabolic doctor will continue to advise you on how often your child should eat as he or she gets older. When they are well, many teens and adults with CTD can go without food for up to 12 hours without problems. The other treatments usually need to be continued throughout life.

3. Diet

Sometimes, in addition to L-carnitine treatment, a low-fat, high carbohydrate food plan is recommended. Any diet changes should be made under the guidance of a dietician familiar with CTD. Ask your doctor whether your child needs to have any changes in his or her diet.

4. If your baby has CTD, call your doctor at the start of any illness

Always call your health care provider when your baby has any of the following:

1. poor appetite
2. low energy or excessive sleepiness
3. vomiting
4. diarrhea
5. an infection
6. a fever
7. persistent muscle pain or weakness

Babies with CTD need to eat extra starchy food and drink more fluids during any illness – even if they may not feel hungry – or they could have a metabolic crisis. Children who are sick often don't want to eat. If they won't or can't eat, they may need to be treated in the hospital to prevent serious health problems. Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

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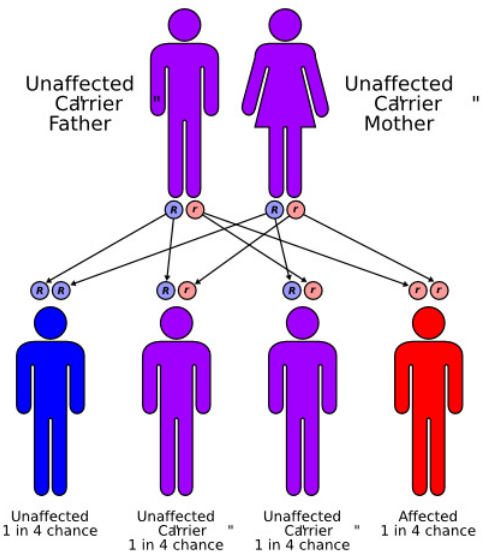
What happens when Carnitine transporter deficiency (CTD) is treated?

With prompt and careful treatment, children with CTD usually live healthy lives with typical growth and development. Treatment with L-carnitine can often reverse heart enlargement and muscle weakness. Babies with CTD who have repeated episodes of metabolic crisis may have permanent brain damage. This can cause learning disabilities or mental retardation.

What causes the CT enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. People with CTD have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the CT enzyme does not work properly or is not made at all.

How is Carnitine transporter deficiency (CTD) inherited?



CTD is inherited in an autosomal recessive manner. It affects both boys and girls equally. Everyone has a pair of genes that make the CT enzyme. In children with CTD, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent. Parents of children with CTD are rarely affected with the disorder. Instead, each parent has a single non-working gene for CTD. They are called carriers. Carriers do not have CTD because the other gene of this pair is working correctly. When both parents are carriers, there is a 25% chance in each pregnancy for the child to have CTD. There is a 50% chance for the child to be a carrier, just like the parents. And, there is a 25% chance for the child to have two working genes.

Genetic counseling is available to families who have children with CTD. Genetic counselors can answer your questions about how CTD is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

What other testing is available?

CTD can be confirmed by a carnitine uptake on a skin sample. Talk to your doctor or genetic counselor if you have questions about genetic testing for CTD.

Can you test during pregnancy?

If both gene changes have been found in the child with CTD, DNA testing can be done during future pregnancies. The sample needed for this test is obtained by either CVS or amniocentesis. If DNA testing would not be helpful, testing during pregnancy can be attempted by performing special tests on fetal cells. Again, the sample needed for these tests is obtained by either CVS or amniocentesis. Parents may either choose to have testing

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during pregnancy or wait until birth to have the baby tested. A genetic counselor can talk to you about your choices and answer other questions you may have about prenatal testing or testing your baby after birth.

Can other members of the family have Carnitine transporter deficiency (CTD) or be carriers?

Having CTD

The brothers and sisters of a baby with CTD have a small chance of being affected, even if they haven't had symptoms. Finding out whether any other children in the family have CTD is important because early treatment may prevent serious health problems. Talk to your doctor or genetic counselor about testing your other children for CTD.

CTD carriers

Brothers and sisters who do not have CTD still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done in people over 18 years of age. Each of the parents' brothers and sisters has a 50% chance to be a CTD carrier. It is important for other family members to be told that they could be carriers. There is a very small chance they are also at risk to have children with CTD. Some states do not offer newborn screening for CTD. However, expanded newborn screening through private labs is available for babies born in states that do not screen for this condition. To learn more about expanded newborn screening, see How to obtain MS/MS. When both parents are carriers, newborn screening results are not sufficient to rule out CTD in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening. During pregnancy, women carrying fetuses with CTD may be at increased risk to develop serious medical problems. Some women carrying fetuses with Fatty Acid Oxidation Disorders have developed:

- excessive vomiting
- abdominal pain
- high blood pressure
- jaundice
- abnormal fat storage in the liver
- severe bleeding

All women with a family history of CTD should share this information with their obstetricians and other health care providers before and during any future pregnancies. Knowing about these risks allows better medical care and early treatment if needed.

Can other family members be tested?

Diagnostic testing for CTD

Brothers and sisters of a baby with CTD can be tested using a special test done on a skin sample or by DNA testing using a blood sample.

How many people have Carnitine transporter deficiency (CTD)?

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About one in every 40,000 babies is born with CTD.

Does Carnitine transporter deficiency (CTD) happen more frequently in a certain ethnic group?

CTD has not been found to occur more often in any particular race, ethnic group, geographical area or country.

Where can I find more information?

Fatty Oxidation Disorders (FOD) Family Support Group

http://www.fodsupport.org

Organic Acidemia Association

http://www.oaanews.org

United Mitochondrial Disease Foundation

http://www.umdf.org

Children Living with Inherited Metabolic Diseases (CLIMB)

http://www.climb.org.uk

Genetic Alliance

http://www.geneticalliance.org

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