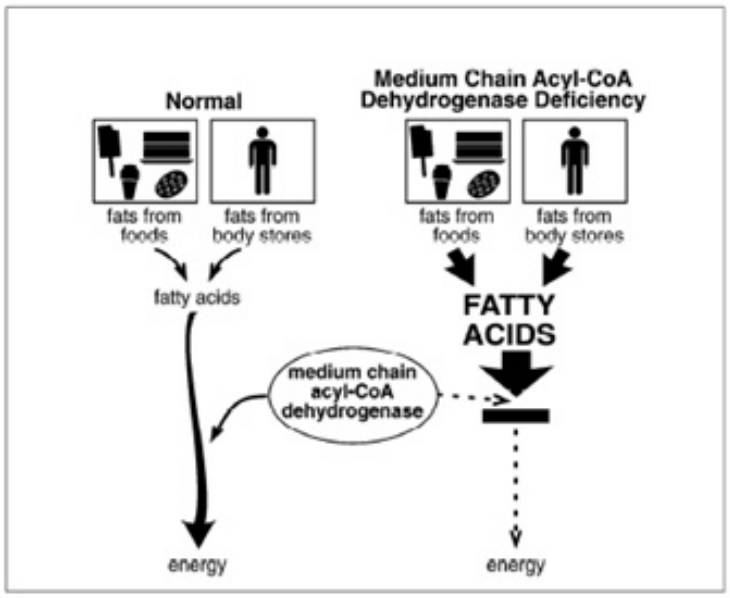
MCADD deficiency
(Medium chain acyl coenzyme A dehydrogenase deficiency)
A fact sheet for parents/carers

What is MCADD deficiency?

MCADD deficiency is a genetic disorder caused by an enzyme deficiency which breaks down fats to give us energy. An enzyme is a protein made in the body, which helps a chemical reaction to proceed. Each of the chemical reactions, or steps, in the bodies' metabolism needs a specific enzyme to function. MCADD is part of a chain of enzymes which act together to break down fats into energy. Babies and children with MCADD deficiency are at danger of developing illness with low blood sugar during episodes of prolonged fasting. MCADD deficiency can cause life-threatening illness.

How does the body normally process fats?



The body normally uses carbohydrates and sugars from our diet for energy and uses fats as an energy reserve. When all of the carbohydrates and sugars in our bodies have been used, we break down fats for energy. One of the enzymes that helps break down fats is called MCADD.

Fat stores in the body. Energy is stored in the body either as a glucose complex (glycogen) or as fat. When we need energy we can use up the glucose stores, after which we need to mobilise the fat stores. These are broken down into fatty acids, which are themselves broken down into shorter lengths ("chain lengths"), each shortening producing energy. Children with MCADD deficiency can break down fat to some extent, but cannot do this very fast, as there is a hold-up at the medium chain length step. If a child tries to break down fats fast, the banked up medium chain fats form toxic substances. Giving glucose will immediately switch off the breakdown of fats.

Symptoms of MCADD

Many children with MCADD are not diagnosed for weeks, months, or even years. The initial symptoms experienced are variable. However, initial symptoms usually occur during infancy or early childhood, and often the first symptomatic episode occurs after a period of fasting.

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Symptoms may include extreme tiredness, skin clamminess, behavior changes, irritability, fever, diarrhea, and vomiting. The affected person may or may not have low blood sugar. If untreated, coma and even death could occur. People with MCADD are normal between episodes of crisis, which are often provoked by periods of fasting without carbohydrate/ glucose supplementation.

With proper treatment, children with MCADD can expect to live typical, healthy lives, with typical growth and development. It is very important to inform everyone involved in your child's medical care that he/she has MCADD, and that he/she receives prompt medical attention during periods of fasting.

Treatment

There are four parts to successful treatment of MCADD:

1. Avoidance of fasting for more than 4-6 hours. When an infant or young child does not eat for more than 4-6 hours, his or her body naturally turns to stored fats for energy. Your child with MCADD lacks the enzyme which converts stored fats into energy. Avoiding fasting has proven to be an effective means of treating MCADD. If your child with MCADD deficiency evenly spaces meals to avoid long periods of fasting, the body will have plenty of energy from food, and will not have to rely on other sources of stored energy. Ask your health provider what is appropriate for your child.

2. A reduced fat, complex carbohydrate food pattern. It should be noted that this is not a fat-free food pattern, but simply low in fats. The body needs small amounts of fat to function properly, and fats should never be completely eliminated from the food pattern. Carbohydrates are the best possible source of energy. They contain many forms of sugar that the body can break down into fuel. If the body can use sugar from food for energy, it won't have to use its precious supply of stored glucose.

3. Supplemental Carnitine. Carnitine is a safe, natural chemical which helps the body produce muscle energy, and also helps remove some breakdown products of fat that children with MCADD cannot process. Children with MCADD may be lacking carnitine. Its use varies with the needs of each individual child. Ask your health provider if carnitine is appropriate for your child.

4. Immediate contact with your child's health provider when illness occurs.

Every child gets sick from time to time. It may be the flu, a cold, an infection, or something more severe. Regardless of the illness, the body uses extra energy in an effort to heal itself. Normally, the body will turn to stored fats for that energy. Again, children with MCADD are unable to use stored fats. Risks after illness and/or fasting include hospitalization, long-term disability and death.

What happens when MCADD is treated?

With prompt and careful treatment, children with MCADD usually live healthy lives with

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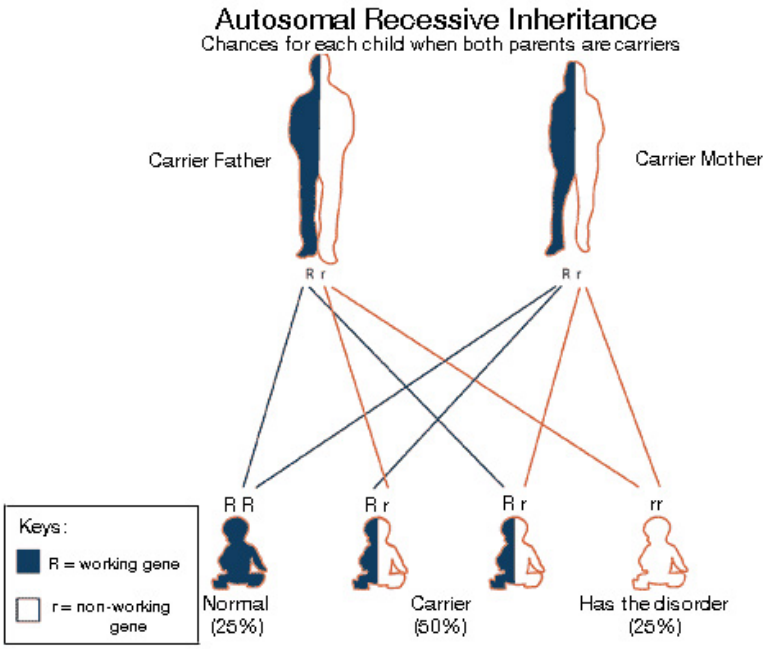
typical growth and development. The goal of treatment is to prevent long-term problems. However, children who have repeated metabolic crises may have life-long learning disabilities, spasticity, chronic muscle weakness or other effects.

How is MCADD inherited?



MCADD is inherited in an autosomal ressesive manner. It affects both boys and girls equally. Everyone has a pair of genes that make the MCADD enzyme. In children with MCADD, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent.

Parents of children with MCADD rarely have the disorder. Instead, each parent has a single non-working gene for MCADD. They are called carriers. Carriers do not have MCADDD 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 MCADDD. 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.

Is genetic testing available?

Genetic testing for MCADD can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause MCADD. In many children with MCADD, both gene changes can be found. However, in other children, only one or neither of the two gene changes can be found, even though we know they are present. DNA testing is not necessary to diagnose your child. It can be helpful for carrier testing or prenatal diagnosis, discussed below. Mutation testing of the gene can help to confirm the diagnosis and for prenatal testing for future pregnancies. However mutation testing limited toe the common A985G mutation will not identify all cases, so a completely normal mutations analysis for this one mutation does NOT rule out a diagnosis of MCADD and a more comprehensive analysis for MCAD mutations may be indicated.

Enzyme assay: MCAD enzymatic activity can be measured in leukocytes and cultured fibroblasts as well as skin, liver, heart, skeletal muscle, and amniocytes using the ETF reduction assay. A frequently employed assay involves acylcarnitine analysis of the medium in cultured

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fibroblasts. The accumulation of C6-C10 acylcarnitines usually confirms the diagnosis. Patients with MCADD usually exibit less than 10% of normal MCAD activity.

What other testing is available?

MCADD can also be confirmed either by a blood test called an acylcarnitine profile or an enzyme test on a skin sample. Talk to your doctor or your genetic counselor if you have questions about testing for MCADD.

Can you test during pregnancy?

If both gene changes have been found in your child with MCADD, 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, an enzyme test can be done during pregnancy on cells from the fetus. Again, the sample needed for this test is obtained by either CVS or amniocentesis. Parents may either choose to have testing during pregnancy or wait until birth to have the baby tested. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

What about my other children/future children?

As MCADD is an inherited condition it is essential to have you other children tested. Children from the same father and mother as the affected infant have a 1 in 4 (25%) chance of having MCADD. Your other children can appear healthy and still have MCADD. If they have MCADD, 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 MCADD it is important to let your obstetrician and pediatrician know that you have a child with MCADD if you are planning future pregnancies so that they may discuss the options with you and prepare accordingly.

How many people have MCADD?

About one in every 15,000 babies is born with MCADD.

When does MCADD deficiency cause problems?

Children have much higher energy requirements than adults, mostly because they are continually growing. Usually, after a meal, to provide the energy to keep us going, our body first uses up the sugar (glucose) which was contained in the meal. This generally lasts for about the first 4 hours, then the body goes on to use stored glucose from the liver, which is called glycogen. The next step involves using stored fat, which is the body's way of storing excess energy from meals. After about 8 hours of fasting, (not eating or drinking anything but water), young children start to break down fat to form ketones, a metabolic fuel, as an energy source. This is very different from adults, who only start to use fat after about 24 hours of fasting.

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Because children with MCADD deficiency cannot make ketones fast enough to provide an alternative source of energy, they rely on glucose, which then gets used up. This is why children with MCADD deficiency usually have low blood glucose, (hypoglycaemia), if they fast for any length of time. Sometimes the low blood sugar causes fits or the child may go into a coma. The coma is partly due to a build-up of substances known as medium chain fatty acids, which can't be broken down, and partly due to low blood sugar. They can get sick before the blood sugar is really low.

However, children with MCADD deficiency are perfectly well so long as they are able to eat regularly and do not get to the stage where the body needs to use these breakdown products of fat. Some children with MCADD deficiency have never been sick, and are only found to have the condition after a brother or sister has been diagnosed.

The major problem for children with MCADD deficiency is when they have a viral illness particularly if there is vomiting and diarrhoea, or a sore throat, which makes small children reluctant to eat or drink. Having a virus means the body requires increased energy to fight off the virus, and children need to eat more often under these conditions, particularly if there is a high temperature. A good rule of thumb is that babies with MCADD deficiency need to feed every 4 hours during the day and every 5-6 hours overnight. By 6 months of age they need to feed regularly during the day and can sleep for no longer than 10 hours overnight. If they are sick, they should be fed every 6 hours at night.

If a child fasts for longer than this, or vomits, or becomes unusually drowsy, the child should be seen promptly by someone who understands the condition, such as the paediatrician or the metabolic doctor who supervises the child's care. The doctors big hospitals with paediatric sections should also be familiar with MCADD deficiency. Even so it is important to take this information sheet to the hospital.

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

PacNoRGG pamphlet: MCAD

http://mchneighborhood.ichp.edu/pacnorgg/media/Metabolic/mcad_eng.pdf

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