

MCADD

Synonyms:

MCADD, Medium chain acyl-CoA dehydrogenase deficiency, medium chain fat oxidation defect and ACADM defect.

Biochemical background:

MCADD is an inherited disease caused by a change on chromosome 1 in the ACADM gene. The disease is inherited by autosomal recessive inheritance. To become ill you must have two defective disease genes – one from each parent. Both parents must be carriers of the mutation.

In every pregnancy there is a 25 % risk that the child inherits the disease when both parents are carriers of the defective gene. There is a 50% probability that the child will inherit only one defective gene and thus become carrier of the disease without having symptoms (like the parents) and 25 % probability that the child does not inherit any defective genes.

Several mutations are known in the ACADM gene, but in many Western European countries a change in position 985 of the gene is far the most common and occurs in 80-90 % of the patients. This is known as classical MCADD but most other mutations will cause identical disease. There are a few mutations, which give a milder course of disease, but they are rare in Denmark.

The change in the ACADM gene renders the MCADD enzyme defective. Enzymes work in the body by promoting the conversion of certain chemical substances; e.g. some enzymes are important in the transformation of food into energy.

MCADD enzymes convert fat into energy. In this process many enzymes work together and MCADD handles only the portion of the fat we call the medium chain fat – i.e. the fat which contains 6-12 carbon atoms. Other fat such as long-chain fat has longer chains of carbon atoms and are converted by other enzymes. When the enzyme MCADD is defective medium chain fat is not converted into energy and instead it accumulates as medium-chain acyl-CoA compounds in the body.

The medium chain fat comes from two sources: Fat from the diet and the fat remaining after the conversion of long chain fat stops.

The consequences of a defective MCADD enzyme are poor formation of energy with risk for low blood glucose (blood sugar) and accumulation of the above mentioned medium chain acyl-CoA compounds. The latter implies a further inhibited energy generation and loss of the substance carnitine. Carnitine is lost because the body tries to detoxify itself of medium-chain acyl-CoA compounds and this process consumes carnitine. A lack of carnitine can worsen the energy generation.

Untreated, a high proportion of children will have periods (crises) with a rapidly progressing effect on the brain with drowsiness, risk of coma (= loss of consciousness) and eventually a fatal outcome. In addition fluid disturbances and low blood glucose can be seen. Crises causes death in 25 % of the patients and of the survivors 25 % will be brain damaged.

The crises can be triggered by:

- Fasting
- Diseases with fever (over 38.5 °C) for example lung infection, otitis media
- Gastrointestinal disorders with diarrhoea and vomiting

Under these circumstances the body has higher energy consumption than normal and are therefore trying to burn fat. To do this, fat is released from the body fat stores, but because medium chain fat cannot be used when you have MCADD, it accumulates in the blood instead. This accumulation together with the energy shortages triggers the symptoms.

Inadequately controlled children who are treated before they have a crisis have a good prognosis.

- Almost all children in Denmark are diagnosed by screening and treated before they develop symptoms – nearly 100 % of these children have normal lifespan, develop normally and have the same prospects as other children.

Treatment consists of a few relatively simple steps, which in turn must be strictly observed

Everyday management when the baby is healthy

- **To reduce the time of fasting there is a need to give regular, frequent meals**
 - o The maximum time between meals is 3-4 hours when the child is 0-6 month old
 - o Afterwards approx. 1 hour each month can be added to the fixed period
 - o At 12 month and onward the maximum fasting is 12 hours
- **General principles of energy distribution of food should be followed i.e. 30 % energy from fat with the following comments:**
 - o We are aware that breast milk contains more than 30 E% but the benefits of breastfeeding outweigh this and probably strict adherence to fasting times is the most essential at this stage of life.
 - o Non-breastfeeding infants who receive infant formulas also get higher fat energy percent. This are accepted up to 6 month of age. From 6 month neither breast milk or formula should be the main diet for the child why the fat energy percent will fall.
- **Generally all food can be used in the diet, as foods with a high MCT content are rare in the Danish diet.**
 - o Coconut and palm kernel oil contains a lot of MCT and should be avoided in large quantities. There are small amounts in e.g. vitamin preparations but there is no problem in taking them.
- **Morning and evening meals should never be skipped**
 - o If a meal is not consumed as planned a drink rich in sugar (carbohydrate) must be given. A content of min. 10 g carbohydrate per 100 ml is appropriate e.g. apple, orange or other fruit juice perhaps with added Maltodextrin e.g. Maxijul or Fantomalt.
 - o All meals should contain starch from e.g. bread, grains, potatoes, rice, pasta
 - o In a very few children we must provide an additional contribution of starch at dinner. It can for example be children who are dull in the morning and apparently have more limited fasting tolerance than other children.
 - o Some children also need extra starch in relation to physical activity.

Special features

- ***The level of carnitine in the blood should be monitored regularly with blood test***
 - If the level are too low carnitine mixture are given for a limited time (usually 2 months) with subsequent measurement of the carnitine levels in the blood at next appointment in the outpatient clinic.
- **Any disease of the child is serious and should be treated promptly to avoid a crisis**
 - There must be strict compliance with the dietary acute regimen (see separate instructions) to prevent energy shortages and burning of fat. The principle of this regimen is frequently offered glucose (sugar) both day and night.
 - If the child normally is treated with carnitine the dose should be doubled while the child is sick
 - If the child is under 6 months the hospital should always be contacted about treatment with glucose directly into a vein.
 - The child should always have open access to the child admittance without first contacting normal emergency services.
- **Vaccinations should be implemented as for other children**
 - After a vaccination some children have mild symptoms including fever of the disease being vaccinated against. Therefore the child must be on fever-reducing medication 1 hour before the vaccination and every 6 hours after vaccination through a total of 2 days.
- **Any procedure requiring anaesthesia should be planned carefully**
 - Children should not fast for too long time and preferably (and always during prolonged procedures) have glucose directly into a vein before, during and after the procedure.
 - The child should be placed first on the program of the day's scheduled operations to minimize the risk of postponement.

The control program will vary. The child will always be followed in collaboration with the child's local children's ward. Often you will see the child at the Clinic for Rare Handicaps at Rigshospitalet each 3-6 months in the first year of life, later once a year is sufficient. At all visits a blood sample for determination of carnitine in the blood will be taken. At one of the first visits blood samples will also be taken from both parents to analyze the ACADM gene. In a few children biopsy of the skin (after a local anaesthetic) can be required.

Your contact doctor
Allan Meldgaard Lund
Department of Clinical Genetics 4062
Juliane Marie Centre
35 45 38 87

Your contact dietician
Camilla Henriksen
Child Nutrition Unit, Dept. 4094
Juliane Marie Centre
35 45 18 62

Helle Vestergaard
Child Nutrition Unit, Dept. 4094
Juliane Marie Centre
35 45 81 61

Age 0-6 months

Fasting period

To limit the fasting, regular frequent meals should be given. The maximum time between meals is 3-4 hours.

Food and energy percentages in the food

The general principles of energy distribution in the diet should be followed, namely

- Children who are breastfed should follow the guidelines that apply to healthy children and breastfed until they are 6 months old
- Children who are not breastfed or only breastfed in part must have general formula corresponding to the age of the child

Both breast milk and infant formula have a relatively high content of fat. Nonetheless it is recommended in this age group because breast milk has many other advantages and partly to ensure the energy needs in this phase where babies grow much.

Age 7-12 month

Fasting period

To limit the fasting, regular frequent meals should be given. The fasting can be increased with approx. 1 hour each month when the child is older than 6 months until the child is 12 months so that:

- at 7 month the maximum fasting is 5-6 hours
- at 8 month the maximum fasting is 6-7 hours
- at 9 month the maximum fasting is 7-9 hours
- at 10 month the maximum fasting is 9-10 hours
- at 11 month the maximum fasting is 10-11 hours
- at 12 month the maximum fasting is 11-12 hours

It should be noted that the maximum fasting could vary considerably from child to child, which needs to be taken into account individually.

Breakfast and dinner should never be skipped.

The energy percentage in the food

The part of dietary energy coming from fat should not exceed 30 % which is a reduction compared to the 30-45 energy percent that is recommended for healthy children without MCADD.

The food

Because of the recommendation to lower fat content the following changes in the diet, usually offered children aged 7-12 months, must be made:

- Skimmed milk is used instead of whole milk in the cup and porridge
- Do not add extra fat to the porridge
- Lactation and/or infant formula may continue but not as the main nutrition
- Fabricated porridge mixture may be used but the fat content should not exceed 5 grams per serving
- Coconut contains a lot of MCT and should therefore be avoided in large quantities. However it can be consumed in the quantities that occur in for example vitamin preparations.

Remember

All main meals should contain starch i.e. slow digesting carbohydrates. This means that all meals, not excluding breast milk or infant formula must contain one or more of the following foods: bread, grain, potatoes, rice or pasta.

That means

- Avoid fat on bread
- Use lean cold cuts products and lean meat i.e. max 10 g fat per 100 g
- Use lean milk and dairy products like skimmed milk and light or cheesy products
- Eat fruit and vegetables

Age 1-2 years

Fasting period

To limit the length of the fasting time regular, frequent meals should be given. The maximum time between meals is 12 hours. It should be noted that the maximum tolerated fast can vary considerably from child to child, which needs to be taken into account individually.

Breakfast and dinner should never be skipped.

The energy percentage in the food

The part of dietary energy coming from fat should not exceed 30 % which is a reduction compared to the 30-45 energy percent that is recommended for healthy children without MCADD.

The food

All main meals should contain starch i.e. slow digesting carbohydrates. This means that all meals, not excluding breast milk or infant formula must contain one or more of the following foods: bread, grain, potatoes, rice or pasta.

That means

- Avoid fat on bread
- Use lean cold cuts products and lean meat i.e. max. 10 g fat per 100 g
- Use lean milk and dairy products like skimmed milk and light or cheesy products
- Eat fruit and vegetables

For hot food you can use the plate model, where the food on your plate should be divided so that approx. 1/5 is meat/fish/eggs/cheese, 2/5 are vegetables and 2/5 is bread/potatoes/rice/pasta.

Remember

All main meals should contain starch i.e. slow digesting carbohydrates. This means that all meals must contain one or more of the following foods: bread, grain, potatoes, rice or pasta.

Avoid

- Everything with coconut i.e. coconut milk, coconut oil and desiccated coconut
 - o Thai food and other exotic dishes with coconut milk
 - o Cakes with coconut flakes for i.e. coconut tops and coconut macaroons
- Palmin
 - o Cakes prepared with or containing palmin i.e. “klejner” and “kiksekage”

Age over 2 years

Fasting period

To limit the length of the fast regular frequent meals should be given. The maximum time between meals is 12 hours. It should be noted that the maximum tolerated fast can vary considerably from child to child, which needs to be taken into account individually.

Breakfast and dinner should never be skipped.

The energy percentage in the food

The part of dietary energy coming from fat should not exceed 30 %, which corresponds to the recommendation for healthy children without MCADD over 2 years and adults. No more than 30 % of the energy must come from fat.

The food

All main meals should contain starch i.e. slow digesting carbohydrates. This means that all meals, must contain one or more of the following foods: bread, grain, potatoes, rice or pasta.

That means

- Avoid fat on the bread
- Use lean cold cuts products and lean meat i.e. Max. 10 g fat per 100 g
- Use lean milk and dairy products like skimmed milk and light or “Cheasy” products
- Eat fruit and vegetables – from 4 years of age 3-5 pieces are recommended per day

For hot food you can use the plate model, where the food on your plate should be divided so that approx. 1/5 is meat/fish/eggs/cheese, 2/5 are vegetables and 2/5 is bread/potatoes/rice/paste.

Remember

All main meals should contain starch i.e. slow digesting carbohydrates. This means that all meals must contain one or more of the following foods: bread, grain, potatoes, rice or pasta.

Avoid

- All food with coconut i.e. Coconut milk, coconut oil and desiccated coconut
 - o Thai food and other exotic dishes with coconut milk
 - o Cakes with coconut flakes for i.e. Coconut tops and coconut macaroons
- Palmin
 - o Cakes prepared with or containing Palmin i.e. “klejner” and “kiksekage”

Young and adults

Fasting period

To limit the length of fast, regular frequent meals should be given. The maximum time between meals is 12 hours. It should be noted that the maximum length of fast tolerated can vary considerably from person to person, which needs to be taken into account individually.

Breakfast and dinner should never be skipped.

The energy percentage in the food

The part of dietary energy coming from fat should not exceed 30 %, which corresponds to the recommendation for healthy young and adults without MCADD. No more than 30 % of the energy must come from fat.

The food

All main meals should contain starch i.e. slow digesting carbohydrates. This means that all meals must contain one or more of the following foods: bread, grain, potatoes, rice or pasta.

That means

- Avoid fat on bread
- Use lean cold cuts and lean meat i.e. Max. 10 g fat per 100 g
- Use lean milk and dairy products like skimmed milk and light or “Cheasy” products
- Eat fruit and vegetables – from 11 years of age a minimum of 600 g fruit and vegetables are recommended per day

For hot food you can use the plate model, where the food on your plate should be divided so that approx. 1/5 is meat/fish/eggs/cheese, 2/5 are vegetables and 2/5 is bread/potatoes/rice/paste.

Remember

All main meals should contain starch i.e. slow digesting carbohydrates. This means that all meals must contain one or more of the following foods: bread, grain, potatoes, rice or pasta.

Avoid

- Everything with coconut i.e. Coconut milk, coconut oil and desiccated coconut
 - o Thai food and other exotic dishes with coconut milk
 - o Cakes with coconut flakes for i.e. Coconut tops and coconut macaroons
- Palmin
 - o Cakes prepared with or containing Palmin i.e. “klejner” and “kiksekage”

Alcohol

Alcohol can be consumed but it inhibits the production of the glucose in the body. When you have MCADD the risk of low blood glucose is increased. Therefore alcohol must be taken together with slowly absorbed carbohydrates, especially just before going to bed. Slow absorbed carbohydrates can be i.e. bread. Your friends should know that you have MCADD and that you must have glucose if it goes wrong.

Calculation of fat energy percentage

Some products state the fat energy percentage, but if this is not the case it can be calculated according to the following formula:

$$\frac{\text{The product's fat content measured in grams per 100 grams} \times 38}{\text{The total energy content of the product in kJ} \times 100} = \text{the fat energy percentage}$$

e.g.

ymer contains 3,5 grams of fat and 300 kJ per 100 grams

these numbers are put into the formula

$$\frac{3,5 \text{ grams of fat} \times 38}{300 \text{ kJ} \times 100} = 44 \%, \text{ i.e., } 44 \% \text{ of the energy in ymer comes from fat.}$$

When choosing which products to include in the diet, it is important that the most frequently consumed products have low fat energy content. Products, which are more rarely consumed, can have higher fat energy content than 30.