kanso

Dr Schär

Long chain fatty acid oxidation disorders: therapy in infants and young children

Foreword

Dear parents,
dear relatives,

Your child has been diagnosed with a disorder of fat metabolism (digestion), i.e. how fats are used for energy by the body. It is unlikely that you will have heard of this kind of illness before, and are rightfully concerned about your child. You will have many questions and, to understand the answers, it is necessary to explain some specialist medical terminology.
Some of you may also be finding it difficult to accept that your child has a genetic metabolic disorder, even though he or she looks completely healthy and shows no symptoms. This brochure should help you understand both the diagnosis and the therapy. We will show you that the therapy can be well integrated into your family life. You will then have the "tools" to be able to live well with the condition.
This brochure, however, can only give you a general overview. Each child is different; therefore, every child must be treated as an individual. Your first point of contact should always be your metabolic team. Generally speaking, a metabolic team consists of specialists from various professional groups. Along with the metabolic specialist (doctor) and the dietician / nutritionist, there is also a psychologist who supports the patient and his / her parents. A social worker may also be available to assist you in getting further support (e.g. request for financial benefits, etc.).

The experienced team in your metabolic centre knows your child and can answer all of your individual questions personally and expertly.

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1 Principles of disorders of energy production from long-chain fatty acids (fatty acid oxidation)

1.1 Metabolism and metabolic disorder

The term **metabolism** comprises all the processes which are necessary for the **development of the body** (e.g. for growth), for **the preservation of bodily functions** and for **energy production**. To fulfil these tasks, the nourishment consumed with food or the reserves built-up in the body are processed in many carefully coordinated stages (chemical reactions). These stages are enabled by **enzymes** and **transporters** (these are proteins produced in the body). Every stage in the metabolism needs its own **enzyme**.

If a particular enzyme does not work properly in the body, the corresponding metabolic stage may also not be carried out properly, and this creates a **metabolic disorder**. Since there are many different metabolic stages, there are also many different metabolic disorders.
The metabolism of fatty acids serves to supply energy for the body and its organs. This is what this brochure explains.

1.2 What are nutrients and why are they important?

A nutrient is something that makes us thrive and grow. The main components of nutrition (macronutrients) are protein, fat and carbohydrates. They mainly provide energy to the body and we need them in large quantities. However, vitamins, minerals and trace elements (micronutrients) are also essential nutrition to our body. Other essential food components are water and fibre.

Fats and fatty acids

The most important function of fat is the supply of energy. Fat has the highest energy density and supplies more than double the calories (energy) of carbohydrates. The body creates fat deposits for fasting periods. But fat is also used as thermal insulation. It is further required as a transporter for fat-soluble vitamins. Foods rich in fat are tastier because many flavourings are fat-soluble. The body can draw fat from two different sources; from food and from fat stored in the body.
Fats consist of glycerine and various fatty acids which are separated from one another during digestion in the intestine. Fats are also called triglycerides due to their structure i.e. one glycerine molecule bonds to three fatty acids. The type of fatty acids they contain determine the property of a fat (e.g. liquid or solid) and its functions in the body e.g. immune.

Fatty acids consist of carbon atom chains of different lengths (carbon atoms are illustrated with the letter C). Based on the chain length, they are classified into 3 groups:

FIGURE 1: Fats and fatty acids

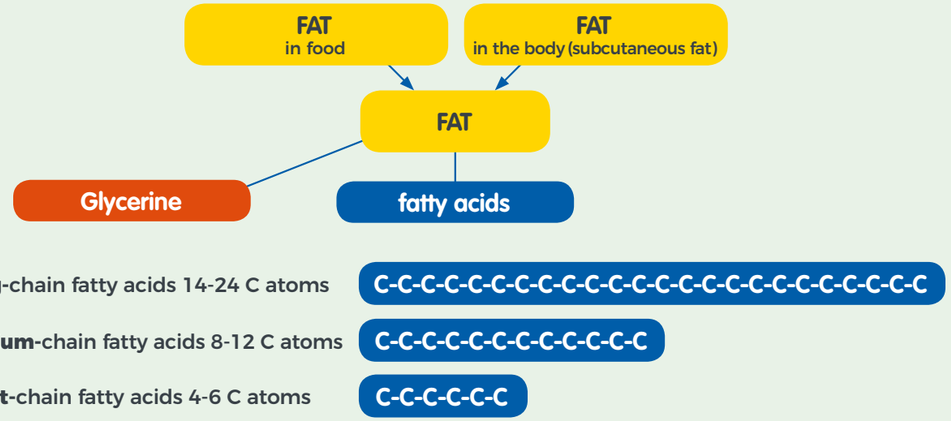
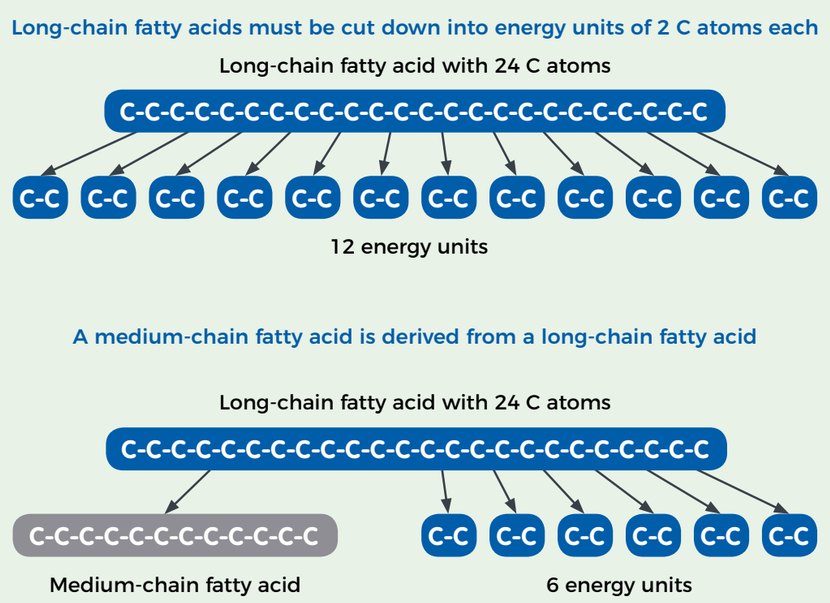


FIGURE 2: Shortening of long-chain fatty acids



The fat found in most foods and body fat are **long-chain fatty acids**. For energy production, long-chain fatty acids are shortened to medium-chain fatty acids. Long-chain fatty acids (illustrated in the figure with a chain of 24 C atoms) are cut down into “energy units” of 2 C atoms each. The long-chain fatty acid is thus shortened to a medium-chain fatty acid by splitting off 6 energy units.

Protein

Protein is made up of amino acid chains. There are 20 common amino acids for human nutrition with 9 of these being essential for consumption. Protein is the basic component of all human cells. Protein builds new cells and repairs existing cells. Hormones and enzymes as well as our immune cells are also made of protein. The body also uses protein as an energy source when the its preferred energy source (glucose) is not available. Protein is contained in animal as well as plant based foods. Animal protein including dairy products are rich sources of protein due to the amino acid composition (containing all 9 essential amino acids). Meat, fish or milk are examples of animal protein. Good sources of vegetable protein are found in pulses, tofu or cereal products.

Carbohydrates (saccharides)

Carbohydrate is a generic term for different types of sugar and starch. They are found in great quantities in plant based foods such as fruit and cereals. These contain types of sugar such as **glucose**, fruit sugar (**fructose**) or starch (large glucose chain). Milk is the only animal food containing carbohydrates in the form of milk sugar (**lactose**). Carbohydrates predominantly supply the body with energy. The brain relies almost exclusively on glucose as an energy supplier. Glucose can be stored in the body as **glycogen** (stored carbohydrate) in the muscle and in the liver. If required, e.g. if a person has not eaten for a long time, the glucose is released again. Glycogen reserves are particularly limited in children and depleted after a short period of time.

Fibres

Fibres are found only in vegetable foods, mostly present in the skins. Wholemeal flours, bread and cereal, fruit, vegetables and pulses contain many fibres. Fibres are not broken down in the small intestine and reach the colon undigested. Fibres contribute to the maintenance and restoration of intestinal structures and functions: normal motility, absorption and immune defences. They retain water, thus increasing the stool volume and preventing blockages. Bacteria located in the intestine can break down soluble fibres. Fibre rich foods may also have beneficial effect on blood sugars and satiety by slowing down absorption of nutrients particularly sugars.

Vitamins

In most cases, the body cannot form vitamins itself. They are vital as they perform hundreds of functions in the body including; wound healing, bone development and are essential for the immune system. Vitamins are found in a vast amount of foods including fruits and vegetables, fish, dairy products and fortified cereals. The body cannot store most water-soluble vitamins (e.g. B vitamins, vitamin C) and eliminates them when there is a surplus. Fat-soluble vitamins (A, D, E and K) can be stored, the body therefore does not depend on a daily intake.

Minerals

Like vitamins, minerals are also vital. They are subdivided into major and trace elements depending on their daily demand. Major elements are calcium, magnesium and sodium. Iron, iodine or selenium are trace elements. They have many functions in the body. They are especially important components of bones and hormones, they also regulate metabolic processes.

1.3 How is fat metabolised and used in the body?

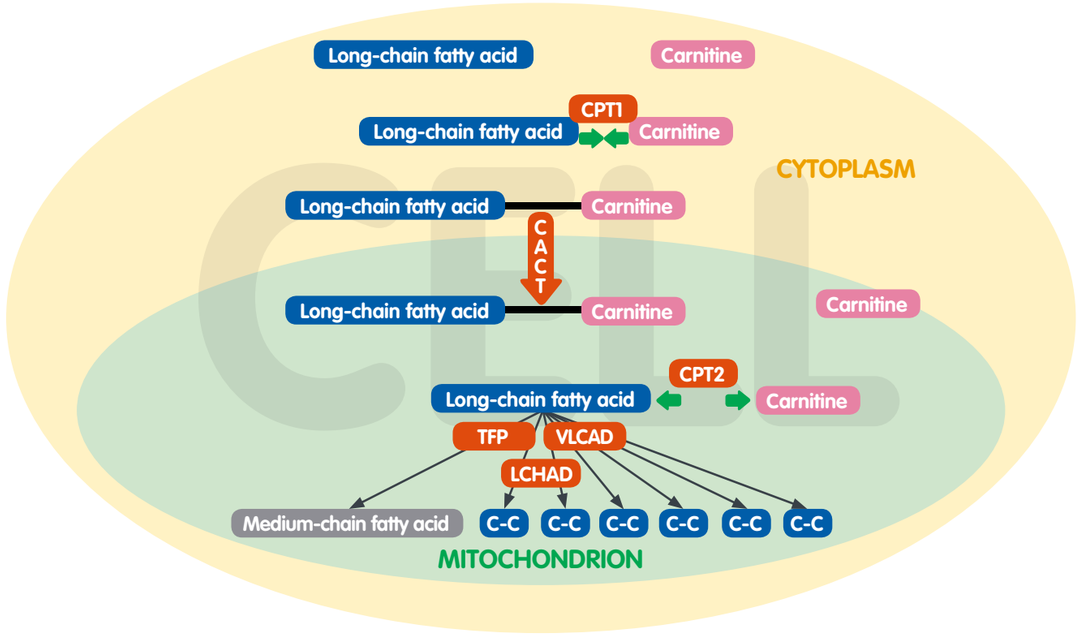
Fat is absorbed as food and used by the body for energy production. The body can also break down its own fat reserves to generate energy. Specific fat elements, so-called essential fatty acids, must be absorbed regularly as food, as they are essential for the development of all cells and for the control of the body's vital processes.

Fat absorbed as food normally consists of **long-chain fatty acids**. These fatty acids can be imaged as chains which are broken down with the aid of **enzymes** so that they can be available for energy production. Energy production from the breakdown of fatty acids is very important for muscles, and especially for the heart muscle.

Enzymes are formed within the body and facilitate metabolic functions. Many different enzymes are involved in the breakdown of fatty acids. Each of these enzymes facilitates an exact breakdown stage and has a very specific function in it. This is illustrated in **FIGURE 3**.

Stage 1: The **long-chain fatty acid** is linked to carnitine by the enzyme CPT1 in the cytoplasm. The link is called **acylcarnitine**.
Stage 2: The **acylcarnitine** is transported by the transporter-enzyme CACT into a subunit of the cell (mitochondrion).
Stage 3: The link (acylcarnitine) is dissolved again by the enzyme CPT2. Carnitin can then return to the cell and be reused here.
Stage 4: The **long-chain fatty acid with 24 C atoms** is shortened to a **medium-chain fatty acid** by the enzymes VLCAD, LCHAD and TFP. This forms 6 "energy units". The shortening of fatty acids is called β oxidation (β is a Greek letter and is called "beta").

FIGURE 3: Shortening of long-chain fatty acids



Medium-chain fatty acids are formed in the breakdown process of long-chain fatty acids. These are, as the name suggest, a little shorter. Medium-chain fatty acids are broken down by an enzyme different to those required in long-chain fatty acids breakdown; for this reason, their processing is not restricted in any of the metabolic disorders described here.
Medium-chain fatty acids do not need to be linked to carnitine, and do not require the transporter enzyme CACT to reach the mitochondrion. This fact can be used in the dietary management of metabolic disorders of long-chain fatty acids.

1.4 What happens with a disorder of energy production from long-chain fatty acids?

If energy production from long-chain fatty acids does not work, **two problems** arise:

1. The body does not have the energy from the breakdown of fatty acids
2. The fatty acids which have not been broken down accumulate in the body

Problem 1: If the body can't gain enough energy from stored **carbohydrates**, energy must be sourced from fat breakdown. Shortly after a meal, the body has enough carbohydrates in the liver and muscles. If these are depleted, the fat reserves must be used for energy production. However, in case of a fatty acid oxidation disorder, the fat reserves cannot be used sufficiently. For this reason, long periods of fasting or an increased energy demand from the body, could result in energy deficiency. This energy deficiency can lead to serious hypoglycaemias (dangerously low concentrations of blood sugar). In hypoglycaemia, the brain is particularly at risk. A reduction in muscle fibres is also a risk if there is a lack sufficient energy, which could lead to muscle pain and weakness but also to problems with the heart muscle longer term.

Problem 2: Long-chain fatty acids are partially bonded with the **carrier substance carnitine** and excreted in the urine. But they can also accumulate and harm the body, particularly the heart. It can lead to cardiac arrhythmias or disorders of the heart's pumping function. Furthermore, there is less carrier substance carnitine is then available to the body.

2 Are there different disorders in the oxidation of long-chain fatty acids?

From image 2 it is clear that there are 6 enzymes required for the metabolism of long-chain fatty acids. Since each of the 6 enzymes can be damaged, there are also 6 metabolic disorders of long-chain fatty acids. CPT1 **deficiency**, CACT **deficiency**, CPT2 **deficiency**, VLCAD **deficiency**, LCHAD **deficiency** and TFP **deficiency**. These metabolic disorders are described individually below. As your child has only one of these disorders, you can skip the descriptions of the others.

Chapter 3 will then describe the dietary management which is mainly the same for all 6 disorders. The information on developmental psychology for families with a chronically ill child also applies to all 6 disorders.

2.1 Very-long-chain acyl-CoA dehydrogenase deficiency (VLCAD deficiency)

What does this mean? The easiest way to explain it is that it is the deficiency of the enzyme named "very-long-chain acyl-CoA dehydrogenase" for the breakdown of long-chain fatty acids. The members of your metabolic team don't usually use the long name, but say VLCAD deficiency. You will no doubt use this abbreviation too.

Incidence: Around 1 in 100,000 to 1 in 50,000 children has a VLCAD deficiency.

Development of the condition: The VLCAD enzyme facilitates the first stage in the actual breakdown (so-called beta-oxidation) of long-chain fatty acids. A disorder of this enzyme means that long-chain fatty acids cannot be used normally for energy production. Furthermore, long-chain fatty acids accumulate in the body and can damage the heart in particular. However, the coupling to carnitine, the transport and the decoupling of carnitine function normally.

Genetics: A VLCAD deficiency is passed on to the child by both parents. This is illustrated in FIGURE 4. The mother and father each carry a defective (RED in the image) and defect-free gene (BLUE in the image) for the VLCAD enzyme. Genes are units in our genome. Each gene contains information for a specific component of the body, e.g. for a special enzyme. Both parents are healthy themselves, because a defect-free gene contains the complete information for the enzyme. But because they have a defective gene, they are called carriers of the enzyme deficiency. If the defective gene is transmitted (passed on) to the child by both parents, the child will have the illness (in the image the child with both red genes). If a parent transmits a blue gene and the other transmits a red gene, then the child will also be a carrier and be healthy like the parents. The child is then naturally also healthy, if a blue gene is passed on by each parent. If both parents are carriers, then the probability that both defective genes are passed on and a child with a VLCAD deficiency is born is 1 out of 4 (a quarter) in each pregnancy. Girls and boys are equally affected.

There is no way of knowing whether you are a carrier of a fatty acid oxidation disorder. This cannot be found out in the check-ups during pregnancy either.

FIGURE 4 **Genetics of the VLCAD gene across three generations**

The image shows that the defective gene was passed onto both parents by their parents (the grandparents), but the grandparents in turn inherited the gene from their parents and so on. **Therefore, being a carrier does not mean that you have done something wrong.**

FIGURE 5 shows the possible situations if a person with a VLCAD deficiency has a child. A distinction must be made between three cases.

Case 1: The partner is not a carrier of a VLCAD deficiency. Then a child is a healthy carrier in each case, since it always inherits a defect-free blue) gene.

Case 2: If the partner is a carrier of a VLCAD deficiency, the probability that the child receives two red genes and therefore has a VLCAD deficiency is 1 out of 2 (half).

Case 3: If both parents have a VLCAD deficiency, then each child will always have exclusively defective (red) genes and a VLCAD deficiency.

FIGURE 5 Genetics in people with a VLCAD deficiency

Diagnosis (Germany): The diagnosis of a VLCAD deficiency is made in the newborn screening. In case of an abnormal result in the newborn screening, common VLCAD deficiency metabolites are then looked for in the blood and urine. A final confirmation of the diagnosis is only possible with an enzymatic and / or genetic examination. An enzymatic examination measures the function of the VLCAD enzyme in a blood sample. A genetic examination searches for changes in the affected gene in the blood.

Disease progression: There are varying degrees of severity of the VLCAD deficiency, depending on how much enzyme is activity there is. In some instances, patients with mild forms do not show any symptoms. Patients with severe progressive forms often have hypoglycaemias. With energy deficiency, there is a risk of muscle pain and of muscle fibre degradation. This can also involve the heart muscle.

Therapy: A distinction is made between **long-term therapy** and **emergency therapy**. **Long-term therapy** consists in the avoidance of long fasting phases, as well as, a mostly low-fat diet with the addition of medium-chain fatty acids (MCT fat). Not all patients require a strict fat restriction; your range of foods is individually determined by your metabolic team.

An **emergency therapy** must be carried out in case of imminent or already occurring metabolic crisis / metabolic dysfunctions, e.g. in case of fever inducing infections, refusal of food or long fasting phases and before surgery / operations. This comprises of a high-dose administration of carbohydrates (e.g. taking a maltodextrin solution whilst still at home) or, if this is not sufficiently possible, via a glucose infusion at your clinic / hospital. It is crucial that an infusion containing fat is not given, as the fat in the infusion solution also contains long-chain fatty acids.

Required check-ups: It is necessary to carry out regular blood tests. Generally speaking, check-ups of the acylcarnitine profile are carried out, i.e. a measurement of the concentration of fatty acids coupled to carnitine and the concentration of carnitine available to the body, as well as tests of the liver and muscles. Concentrations of essential fatty acids also need to be checked to ensure they are sufficient. In some instances, regular blood sugar tests may also be carried out. Other laboratory tests may be necessary depending on each individual case. Your metabolic team will provide you with more information on this. Dietary records, must be checked regularly to ensure overall nutritional intake is as balanced as possible as well as having sufficient vitamins and minerals despite the necessary low-fat diet. . Weight and height are important measurement parameters to ensure each patient is growing adequately. Regular heart examinations will also be carried out.

2.2 Long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency (LCHAD deficiency) / trifunctional protein deficiency (TFP deficiency)

What does this mean? The easiest way to explain it is that it is a deficiency of the enzyme named “long-chain acyl-CoA dehydrogenase” for the breakdown of long-chain fatty acids. The members of your metabolic team don’t usually use the long name, but say LCHAD deficiency. You will no doubt use this abbreviation too. The trifunctional protein is an enzyme complex which consists of 3 parts (therefore tri=three-functional protein). It is also important to remember the abbreviation TFP deficiency here.

Incidence: Around 1 in 150,000 children has a LCHAD or TFP deficiency.

Development of the condition: The LCHAD enzyme facilitates the third stage in the breakdown of long-chain fatty acids (so called beta-oxidation). In case of TFP deficiency, the LCHAD enzyme and two other enzymes are affected. A disorder of the enzyme or the enzyme complex means that long-chain fatty acids cannot be used normally for energy production. Furthermore, long-chain fatty acid residues acids accumulate in the body and can damage the heart in particular. However, the coupling of fatty acids to carnitine, the transport and the decoupling of fatty acids from carnitine function normally.

Genetics: A LCHAD deficiency or a TFP deficiency is passed on to the child by both parents. This is illustrated in **FIGURE 6**. The mother and father each carry a defective (RED in the image) and defect-free gene (BLUE in the image) for the LCHAD enzyme / the TFP enzymes. Genes are units in our genome. Each gene contains information for a specific component of the body, e.g. for a special enzyme. Both parents are healthy themselves, because a defect-free gene contains the complete information for the enzyme. But because they have a defective gene, they are called carriers of the enzyme deficiency. If the defective gene is transmitted (passed on) to the child by both parents, the child will have the illness (in the image the child with both red genes). If a parent transmits a blue gene and the other transmits a red gene, then the child will also be a carrier and be healthy like the parents. The child is then naturally also healthy, if a blue gene is passed on by each parent. If both parents are carriers, then the probability that both defective genes meet and a child with a LCHAD deficiency / TFP deficiency is born is 1 out of 4 (a quarter) in each pregnancy. Girls and boys are equally affected. There is no way of knowing whether one is a carrier of a fatty acid metabolism disorder. This cannot be found out in the check-ups during pregnancy either.

FIGURE 6 **Genetics of the LCHAD gene / TFP gene across three generations**

The image shows that the defective gene was passed onto both parents by their parents (the grandparents), but the grandparents in turn inherited the gene from their parents and so on. **Therefore, being a carrier does not mean that you have done something wrong.**

FIGURE 7 shows the possible situations if a person with a LCHAD deficiency / TFP deficiency has a child. A distinction must be made between three cases.

Case 1: The partner is not a carrier of a LCHAD deficiency / TFP deficiency. Then a child is a healthy carrier in each case, since it always inherits a defect-free (blue) gene.

Case 2: If the partner is a carrier of a LCHAD deficiency / TFP deficiency, the probability that the child receives two red genes and therefore has a LCHAD deficiency / TFP deficiency is 1 out of 2 (half).

Case 3: If both parents have a LCHAD deficiency / TFP deficiency, then each child will always have exclusively defective (red) genes and a LCHAD deficiency / TFP deficiency.

FIGURE 7 **Genetics in people with a LCHAD deficiency / TFP deficiency**

Diagnosis (Germany): The diagnosis of a LCHAD deficiency / TFP deficiency is made in the newborn screening. In case of a conspicuous result in the newborn screening, typical LCHAD deficiency / TFP deficiency metabolites are then looked for in the blood and urine. A final confirmation of the diagnosis is only possible with an enzymatic and / or genetic examination. A genetic examination searches for changes in the affected genes in the blood. An enzymatic examination measures the function of the enzyme in cells from a skin biopsy or a blood sample.

Disease progression: Generally speaking, a LCHAD or TFP deficiency is a severe disorder in the oxidation of long-chain fatty acids. Some children already become seriously ill in the first few days of life. They are at risk of hypoglycaemias which could be life-threatening. With energy deficiency, muscle pain and muscle cell degradation may occur. This can also involve the heart muscle
Non-broken down metabolites accumulate, which could have a toxic effect on the heart, the retina of the eye and the nerves. Cardiac arrhythmias, vision disorders and sensitivity disorders in the arms and legs may occur.
Mothers that are carriers of the LCHAD deficiency can develop a type of “pregnancy poisoning” (HELLP syndrome), a severe pregnancy complication in the last trimester, if the child has an LCHAD deficiency.

Therapy: A distinction is made between a **long-term therapy** and an **emergency therapy**. **Long-term therapy** consists in the avoidance of long fasting phases, as well as in a low-fat diet with the addition of medium-chain fatty acids (MCT fat) and essential fatty acids. Generally speaking, a strictly low-fat diet is required. Your range of foods is individually determined by your metabolic team.
An **emergency therapy** must be carried out in case of imminent or already occurred metabolic crisis, e.g. in case of febrile infections, refusal of food or long fasting phases and before operations. Emergency therapy comprises the administration of many carbohydrates (e.g. by taking a malto-dextrin solution at home) or, if this is not sufficiently possible, via a glucose infusion at the clinic. It is crucial that a fat infusion is not given, since the fat in the infusion solution also consists of long-chain fatty acids.

Required check-ups: It is necessary to carry out regular blood tests. Generally speaking, check-ups of the acylcarnitine profile are carried out, i.e. a measurement of the concentration of fatty acids coupled to carnitine and the concentration of carnitine available to the body, as well as tests of the liver and muscle values. It can also be checked whether the levels of essential fatty acids are sufficiently high. In some instances, regular blood sugar tests are carried out. Other laboratory tests may be necessary depending on each individual course. Your metabolic team provides you with information about this. Through the analysis of dietary records, it must be regularly checked whether the diet is as balanced as possible despite the necessary low-fat nutrition, and whether the child receives sufficient calories through the low-fat diet. Weight and growth are important measurement parameters here.
Regular heart and eye check-ups should be carried out. If sensitivity disorders occur, special nerve check-ups are required.

2.3 Carnitine palmitoyltransferase I deficiency (CPT I deficiency)

What does this mean? It is a deficiency of the enzyme named "carnitine palmitoyl transferase I". The name means that the enzyme is there to carry something, to "transfer". The enzyme facilitates the coupling of long-chain fatty acids to carnitine. The members of your metabolic team don't usually use the long name, but say CPT I deficiency. You will no doubt use this abbreviation too.

Incidence: The illness is very rare, its precise incidence is not known.

Development of the condition: The CPT I enzyme links long-chain fatty acids with carnitine. The fatty acids can only reach the mitochondrion, the place where they are broken down, when linked in this way. A disorder of the enzyme means that long-chain fatty acids cannot reach the place where they are broken down and, as a consequence, they are not or not sufficiently available for energy production. However, the transport, the decoupling of fatty acids from carnitine and the actual breakdown of fatty acids function normally.

Genetics: A CPT I deficiency is passed on to the child by both parents. This is illustrated in **FIGURE 8**. The mother and father each carry a defective (RED in the image) and defect-free gene (BLUE in the image) for the CPT I enzyme. Genes are units in our genome. Each gene contains information for a specific component of the body, e.g. for a special enzyme. Both parents are healthy themselves, because a defect-free gene contains the complete information for the enzyme. But because they have a defective gene, they are called carriers of the enzyme deficiency. If the defective gene is transmitted (passed on) to the child by both parents, the child will have the illness (in the image the child with both red genes). If a parent transmits a blue gene and the other transmits a red gene, then the child will also be a carrier and be healthy like the parents. The child is then naturally also healthy, if a blue gene is passed on by each parent. If both parents are carriers, then the probability that both defective genes meet and a child with a CPT I deficiency is born is 1 out of 4 (a quarter) in each pregnancy. Girls and boys are equally affected.

There is no way of knowing whether one is a carrier of a fatty acid metabolism disorder. This cannot be found out in the check-ups during pregnancy either.

FIGURE 8 Genetics of the CPT I gene across three generations

The image shows that the defective gene was passed onto both parents by their parents (the grandparents), but the grandparents in turn inherited the gene from their parents and so on. **Therefore, being a carrier does not mean that you have done something wrong.**

FIGURE 9 shows the possible situations if a person with a CPT I deficiency has a child. A distinction must be made between three cases.

Case 1: The partner is not a carrier of a CPT I deficiency. Then a child is a healthy carrier in each case, since it always inherits a defect-free (blue) gene.

Case 2: If the partner is a carrier of a CPT I deficiency, the probability that the child receives two red genes and therefore has a CPT I deficiency is 1 out of 2 (half).

Case 3: If both parents have a CPT I deficiency, then each child will always have exclusively defective (red) genes and a CPT I deficiency.

FIGURE 9 Genetics in people with a CPT I deficiency

Diagnosis (Germany): The diagnosis of a CPT I deficiency is made in the newborn screening. In case of a conspicuous result in the newborn screening, typical CPT I deficiency metabolites are then looked for in the blood. A final confirmation of the diagnosis is only possible with an enzymatic and / or genetic examination. A genetic examination searches for changes in the affected gene in the blood. An enzymatic examination measures the function of the enzyme in cells from a skin biopsy.

Disease progression: With a CPT I deficiency, the patient is at risk of severe hypoglycaemias. In a metabolic crisis, patients develop a liver dysfunction which can be very serious. Involvement of the muscles or the heart is not known.

Therapy: A distinction is made between a **long-term therapy** and an **emergency therapy**. **Long-term therapy** consists in the avoidance of long fasting phases, as well as in a low-fat diet with the addition of medium-chain fatty acids. Not all patients require such a strict fat restriction; your range of foods is individually determined by your metabolic team.

An **emergency therapy** must be carried out in case of imminent or already occurred metabolic crisis, e.g. in case of febrile infections, refusal of food or long fasting phases and before operations. This comprises the administration of sufficient carbohydrates (e.g. by taking a maltodextrin solution at home) or, if this is not sufficiently possible, via a glucose infusion at the clinic. It is crucial that a fat infusion is not given, since the fat in the infusion solution also consists of long-chain fatty acids.

Required check-ups: It is necessary to carry out regular blood tests. Generally speaking but particularly in the event of an imminent metabolic crisis, liver values and blood coagulation tests must be carried out (as coagulation factors are also produced in the liver). In some instances, regular blood sugar tests are carried out. In acylcarnitine profile check-ups, an increased level of free carnitine is evident, which is typical of the illness. This is due to the fact that, with the enzyme deficiency, carnitine is not coupled to long-chain fatty acids, and is therefore present in increased quantities in the body. It can also be checked whether the levels of essential fatty acids are sufficiently high. Other laboratory tests may be necessary depending on each individual course. Your metabolic team provides you with information about this. Through the analysis of dietary records, it must be regularly checked whether the diet is as balanced as possible despite the necessary low-fat nutrition, and whether the child receives sufficient calories through the low-fat diet. Weight and growth are important measurement parameters here.

2.4 Carnitine palmitoyltransferase II deficiency (CPT II deficiency)

What does this mean? It is a deficiency of the enzyme named "carnitine palmitoyl transferase II". Transferase means that the enzyme is there to "transfer" something, in this case in the sense of delivering something. The enzyme assists in detaching the bond between fatty acids and carnitine. The members of your metabolic team don't usually use the long name, but say CPT II deficiency. You will no doubt use this abbreviation too.

Incidence: The illness is very rare, its precise incidence is not known.

Development of the condition: The CPT II enzyme separates the fatty acid from the carnitine again at the site of fatty acid oxidation, and the fatty acid is then available for breakdown. A disorder of the enzyme means that the long-chain fatty acids remain linked to carnitine and therefore cannot be used for energy production. Long-chain fatty acid residues cannot be sufficiently broken down accumulate in the body and can damage the heart in particular. However, the coupling of fatty acids to carnitine, the transport to the breakdown site and the actual breakdown of fatty acids function normally.

Genetics: A CPT II deficiency is passed on to the child by both parents. This is illustrated in **FIGURE 10.** The mother and father each carry a defective (RED in the image) and defect-free gene (BLUE in the image) for the CPT II enzyme. Genes are units in our genome. Each gene contains information for a specific component of the body, e.g. for a special enzyme. Both parents are healthy themselves, because a defect-free gene contains the complete information for the enzyme. But because they have a defective gene, they are called carriers of the enzyme deficiency. If the defective gene is transmitted (passed on) to the child by both parents, the child will have the illness (in the image the child with both red genes). If a parent transmits a blue gene and the other transmits a red gene, then the child will also be a carrier and be healthy like the parents. The child is then naturally also healthy if a blue gene is passed on by each parent.
If both parents are carriers, then the probability that both defective genes meet and a child with a CPT II deficiency is born is 1 out of 4 (a quarter) in each pregnancy. Girls and boys are equally affected.

There is no way of knowing whether one is a carrier of a fatty acid metabolism disorder. This cannot be found out in the check-ups during pregnancy either.

FIGURE 10 Genetics of the CPT II gene across three generations

The image shows that the defective gene was passed onto both parents by their parents (the grandparents), but the grandparents in turn inherited the gene from their parents and so on. **Therefore, being a carrier does not mean that you have done something wrong.**

FIGURE 11 shows the possible situations if a person with a CPT II deficiency has a child. A distinction must be made between three cases.

Case 1: The partner is not a carrier of a CPT II deficiency. Then a child is a healthy carrier in each case, since it always inherits a defect-free (blue) gene.

Case 2: If the partner is a carrier of a CPT II deficiency, the probability that the child receives two red genes and therefore has a CPT II deficiency is 1 out of 2 (half).

Case 3: If both parents have a CPT II deficiency, then each child will always have exclusively defective (red) genes and a CPT II deficiency.

FIGURE 11 Genetics in people with a CPT II deficiency

Diagnosis (Germany): The diagnosis of a CPT II deficiency is made in the newborn screening. In case of a conspicuous result in the newborn screening, typical CPT II deficiency metabolites are then looked for in the blood. A final confirmation of the diagnosis is only possible with an enzymatic and / or genetic examination. A genetic examination searches for changes in the affected gene in the blood. An enzymatic examination measures the function of the enzyme in cells from a blood sample or a skin biopsy.

Disease progression: There are various severe progressive forms of a CPT II deficiency. In its most severe form, symptoms are already evident in the first few days of life. Newborns can have life-threatening hypoglycaemias, life-threatening myocardial disorders, cardiac arrhythmias and liver involvement. Additional kidney malformations are typical of the most severe progressive forms; other congenital malformations can also occur. The life expectancy of these children is significantly reduced; many patients pass away in the first few months of life. In some instances, symptoms do not immediately occur in the newborn stage but first appear in the first few months of life. These children often do not have any accompanying malformations. However, the course of the illness is also serious, with severe hypoglycaemias, heart and liver involvement. Milder progressive forms are known, which in some instances first become noticeable at an adult age with symptoms in the muscles, e.g. muscle pain or muscle weakness.

Therapy: A distinction is made between a **long-term therapy** and an **emergency therapy**.
Long-term therapy consists in the avoidance of long fasting phases, as well as in a mostly low-fat diet with the addition of medium-chain fatty acids. Not all patients require such a strict fat restriction! A very low-fat diet is necessary in its severe form. Your range of foods is individually determined by your metabolic team.
An **emergency therapy** must be carried out in case of imminent or already occurred metabolic crisis, e.g. in case of febrile infections, refusal of food or long fasting phases and in case of operations. This comprimises a high-dose administration of sufficient carbohydrates (e.g. by taking a malto-dextrin solution at home) or, if this is not sufficiently possible, via a glucose infusion at the clinic. It is crucial that a fat infusion is not given, since the fat in the infusion solution also consists of long-chain fatty acids.

Required check-ups: It is necessary to carry out regular blood tests. Generally speaking, check-ups of the acylcarnitine profile are carried out, i.e. measurements of the concentration of fatty acids coupled to carnitine and the concentration of carnitine available to the body, as well as tests of the liver and muscle values. Blood sugar tests are carried out during visits to the clinic / hospital. If hypo-glycaemias occur frequently, it is also recommended that blood sugar tests are completed at home It can also be checked whether the levels of essential fatty acids in the blood are sufficiently high. Other laboratory tests may be necessary depending on each individual course. Your metabolic team provides you with information about this. Through the analysis of dietary records, it must be checked whether the diet is as balanced as possible despite the necessary low-fat nutrition, and whether the child receives sufficient calories through the low-fat diet. Weight and growth are important measurement parameters here. It is necessary to carry out regular heart check-ups. Due to the risk of severe cardiac arrhythmias, in some instances children are also checked at home on a monitor.

2.5 Carnitine-acylcarnitine translocase deficiency (CACT deficiency)

What does this mean? It is a deficiency of a transporter named “carnitine-acylcarnitine translocase”. This transporter transports fatty acids linked to carnitine. The members of your metabolic team don’t usually use the long name, but say CACT deficiency. You will no doubt use this abbreviation too.

Incidence: The illness is very rare, its precise incidence is not known.

Development of the condition: CACT transports long-chain fatty acids linked to carnitine to the place where they are broken down. A disorder of the transporter means that long-chain fatty acids cannot reach the place where they are broken down and, as a consequence, they cannot or cannot sufficiently be used for energy production. Furthermore, long-chain fatty acid residues accumulate in the body and can damage the body, particularly, the heart. The coupling of fatty acids to carnitine, the decoupling and the actual breakdown of fatty acids function normally with a CACT deficiency.

Genetics: A CACT deficiency is passed on to the child by both parents. This is illustrated in **IMAGE 12.** The mother and father each carry a defective (RED in the image) and defect-free gene (BLUE in the image) for the CACT enzyme. Genes are units in our genome. Each gene contains information for a specific component of the body, e.g. for a special enzyme. Both parents are healthy themselves, because a defect-free gene contains the complete information for the enzyme. But because they have a defective gene, they are called carriers of the enzyme deficiency. If the defective gene is transmitted (passed on) to the child by both parents,
the child will have the illness (in the image the child with both red genes). If a parent transmits a blue gene and the other transmits a red gene, then the child will also be a carrier and be healthy like the parents. The child is then naturally also healthy if a blue gene is passed on by each parent. If both parents are carriers, then the probability that both defective genes meet and a child with a CACT deficiency is born is 1 out of 4 (a quarter) in each pregnancy. Girls and boys are equally affected.

There is no way of knowing whether one is a carrier of a fatty acid metabolism disorder. This cannot be found out in the check-ups during pregnancy either.

FIGURE 12 Genetics of the CACT gene across three generations

The image shows that the defective gene was passed onto both parents by their parents (the grandparents), but the grandparents in turn inherited the gene from their parents and so on. **Therefore, being a carrier does not mean that you have done something wrong.**

FIGURE 13 shows the possible situations if a person with a CACT deficiency has a child. A distinction must be made between three cases.

Case 1: The partner is not a carrier of a CACT deficiency. Then a child is a healthy carrier in each case, since it always inherits a defect-free (blue) gene.

Case 2: If the partner is a carrier of a CACT deficiency, the probability that the child receives two red genes and therefore has a CACT deficiency is 1 out of 2 (half).

Case 3: If both parents have a CACT deficiency, then each child will always have exclusively defective (red) genes and a CACT deficiency.

FIGURE 13 **Genetics in people with a CACT deficiency**

Diagnosis (Germany): The diagnosis of a CACT deficiency is made in the newborn screening. In case of a conspicuous result in the newborn screening, typical CACT deficiency metabolites are then looked for in the blood and urine. A final confirmation of the diagnosis is only possible with an enzymatic and / or genetic examination. A genetic examination searches for changes in the affected gene in the blood. An enzymatic examination measures the function of the enzyme in cells from a skin biopsy.

Disease progression: A CACT deficiency is mostly a very severe illness. Many patients suffer from a metabolic crisis in the first few days of life; newborns often fall into a coma. Typical symptoms are severe hypoglycaemias and liver and heart involvement with a limited heart function and cardiac arrhythmias. Life expectancy can be poor, with many patients passing away in the first few months of life. However, milder cases are also known with a later onset of symptoms and a less severe progression.

Therapy: Children with a CACT deficiency receive carnitine continuously. From a nutritional point of view, a distinction is made between a **long-term therapy** and an **emergency therapy**.
Long-term therapy consists in the avoidance of long fasting phases, as well as in a low-fat diet with the addition of medium-chain fatty acids (MCT fat). Generally speaking, a strict restriction of the fat supply is required. The range of foods is individually determined by your metabolic team.
An **emergency therapy** must be carried out in case of imminent or already occurring metabolic crisis, e.g. in case of febrile infections, refusal of food or long fasting phases and before operations. This comprimises a high-dose administration of sufficient carbohydrates (e.g. by taking a maltodextrin solution at home) or, if this is not sufficiently possible, via a glucose infusion at the clinic. It is crucial that a fat infusion is not given, since the fat in the infusion solution also consists of long-chain fatty acids.

Required check-ups: It is necessary to carry out regular blood tests. Generally speaking, check-ups of the acylcarnitine profile are carried out, i.e. a measurement of the concentration of fatty acids coupled to carnitine and the concentration of carnitine available to the body. The liver and muscle values are tested. Blood sugar tests are carried out during visits to the clinic; if hypoglycaemias occur frequently, it is also recommended to do blood sugar tests at home. It can also be checked whether the levels of essential fatty acids in the blood are sufficiently high. Other laboratory tests may be necessary depending on each individual course. Your metabolic team provides you with information about this. Through the analysis of dietary records, it must be checked whether the diet is as balanced as possible despite the necessary low-fat nutrition, and whether the child receives sufficient calories through the low-fat diet. Weight and growth are important measurement parameters here. It is necessary to carry out regular heart check-ups. Due to the risk of severe cardiac arrhythmias, in some instances children are also checked at home on a monitor.

3 How can a disorder in the oxidation of long-chain fatty acids be managed?

There are three ways of “managing” dysfunctional fatty acid oxidation:

1. Avoiding long periods of fasting

When long periods of fasting are avoided, the body continues to use carbohydrate reserves as the main energy source and energy production is not required to take place from the breakdown of long-chain fatty acids. Therefore, if you eat a balanced diet at regular intervals, there will always be enough carbohydrates reserves from which energy can be gained. Regular meals are are not normally a problem, as long as the child with a fatty acid oxidation disorder is healthy. The risk occurs when the child has an illness e.g. a fever inducing infection, as the bodyrequires more energy than healthy condition, especially important as some children may not want to eat or drink much or at all.

2. Low-fat diet

A low-fat diet is required to avoid the accumulation of long-chain fatty acids in the body.

3. Use of medium-chain fatty acids

Long-chain fatty acids can be replaced by medium-chain fatty acids (MCT), which are used for energy production without any subsequent fatty acid build-up. (See section on dietary therapy)

3.1 What does daily therapy look like?

The **long-term therapy** of disorders in the oxidation of long-chain fatty acids is the **diet therapy**.

This has the following objectives:

- Normal mental and physical development
- Age-appropriate weight gain
- Age-appropriate growth
- Avoidance of symptoms, e.g. muscle pain
- Avoidance of long-term effects such as heart muscle damage
- Avoidance of catabolic (deteriorating) metabolic situations which could lead to metabolic crises with hypoglycaemias and muscle cell degradation

To reach these objectives, the diet therapy must meet the following requirements:

- Sufficient intake of protein, essential fatty acids, vitamins and minerals
- Meet energy requirements
- Avoid long periods of fasting
- Reduction of long chain fatty acid intake
- Age-appropriate, i.e. melas acceptable to a child
- Tasty dishes
- Suitable for everyday life

You can find detailed information on the practical implementation of the diet in chapter 3.6.

3.2 What does the emergency therapy for the prevention or dietary management of a metabolic crisis look like?

Whenever the body requires more energy than it has available, i.e. due to infection, refusal of food or other situations which could lead to an energy deficiency, there is a risk of **metabolic crisis**. This also includes situations in which the body requires a particularly high amount of energy e.g. in case of heavy physical strain, such as sport. Metabolism is then no longer in balance. A metabolic crisis is considered a situation in which clinical problems and abnormal laboratory values occur.

Typical symptoms of a metabolic crisis are tiredness and fatigue. In all fatty acid oxidation disorders there is a risk of hypoglycaemia, i.e. low blood sugar levels. **If blood sugar levels are too low, the body lacks energy.** In the case of severe hypoglycaemia, the brain in particular can be permanently damaged. Typical symptoms of hypoglycaemia are sweating, restlessness, shaking, ravenous appetite , nausea and tiredness. Seizures may also occur in case of extremely low blood sugars. There are, however, some instances where hypoglycaemia also occurs without any typical symptoms. Discuss with your treatment team whether blood sugar tests may be useful in times of illness / metabolic risk.

In patients with a tendency towards frequent hypoglycaemia, regular blood sugar measurements are recommended at home before meals; but, for most patients, blood sugar levels out with metabolic crisis are perfectly stable, therefore no regular tests are necessary at home. Along with hypoglycaemia, an increase in liver enzyme levels could also indicate metabolic crisis. Energy deficiency combined with an increased level of the enzyme found in muscle; creatine kinase (CK) indicates muscle degradation and may cause muscle pain.
A high-dose intake of carbohydrates is therefore needed in order to prevent the occurrence of a metabolic crisis and it also serves the therapy of a metabolic crisis. Your treatment team will instruct you on what to do yourself in case of infection or refusal of food at home, and when you should visit a clinic / hospital. When oral food intake is reduced, you should give your child drinks rich in carbohydrates e.g. maltodextrin solution or tea / water with sugar. If this is not possible because your child refuses to drink them, carbohydrates can be given via a tube placed into the stomach (naso-gastric) or as a drip in the clinic / hospital. When a drip is used as therapy, there is generally no more risk of hypoglycaemia as long as sufficient amounts of carbohydrates are provided. It is important to know that not every drip / infusion solution contains enough carbohydrates for the treatment of your child with a fatty acid oxidation disorder.

The carbohydrate quantities required depend on the age and weight of the patient and are individually calculated by your treatment team. In case of emergency treatment in a clinic / hospital other than the treating metabolic centre, a **consultation with the metabolic team** is necessary to determine the required emergency therapy. This is the ONLY way it can be guaranteed that there is a sufficient amount of energy provided via the drip / infusion.
It is crucial that a fat infusion is not given, as the fat in the drip / infusion solution also consists of long chain fatty acids.

Emergency health card

Children with a fatty acid oxidation disorder receive an emergency health card from the treating metabolic centre. The emergency health card contains information on how to act in each situation whether is be refusal of food, infections and operations. It also contains the contact details of the relevant metabolic centre and should always be kept near the child. If the child goes to nursery / school, the emergency health card should be kept in the child's bag. An up-to-date copy should also be stored at the nursery / school.

3.3 Recommendations in the event of dietary mistakes, vaccinations and operations

What happens in case of a singular or partial deviation from the dietary management recommendations?

Exceeding the maximum fasting period cannot always be avoided in everyday life. Infants and small children do not always want to eat or drink at an exact time. Exceeding the the recommended fasting period by a small amount of time is not a problem. However, please discuss whichfasting phases can be tolerated with your treatment team and what you should do if your child does refuses to have a meal. A one-off **dietary mistake** (eating food very rich in fat) is not likely to lead to any acute problems. This information is particularly important for other carers (grandparents, teachers, friends' parents etc.). Despite this, deviations from your specialist teams dietary recommendations cannot happen on a regular basis, as a strict implementation of dietary therapy is significant for the long-term course of the illness.

Vaccinations

A side effect of having vaccinations can be fever, which may potentially lead to a metabolic crisis. However, vaccinations prevent illnesses that are much more severe and dangerous than the temporary side effects of a vaccination. It is therefore strongly recommended to vaccinate children with a fatty acid metabolism disorder. In the event of fever after a vaccination, the same recommendations apply as those for fever inducing infections.

Operations

Operations / surgery should always be carried out in collaboration with a metabolic centre, so that the child can be given optimal care before, during and after the operation.
Outpatient operations / surgery is not advisable, as it generally cannot be guaranteed that sufficient carbohydrate drip / infusion therapy is given before and after the operation, as required. In the event of emergency operations, the treating doctors on the ward and the anaesthetist should be informed that the patient has a fatty acid oxidation disorder. The emergency health card should be provided, and the managing doctors should be encouraged to contact the dietary metabolic team to guarantee optimal care.

3.4 When should you take your child to see a health care professional?

As the severity of fatty acid oxidation disorders can vary considerably, it is difficult to make general statements on when you should take your child to the clinic / hospital.

Your treatment team knows your child best and can make individual recommendations based on the severity of the illness and on the former course. It is important to discuss when to contact your specialist team at an early stage, to ensure you are clear on who, when and where to contact in any situation. In patients with a milder form of a fatty acid oxidation disorder, an emergency therapy can be tried at home first e.g. in fever inducing infections, while an immediate / emergency inpatient admission may be necessary for children with very severe cases of the disorder. If, however, an agreed home emergency therapy plan is not able to be completed for any reason, you must contact your metabolic team or take your child to the clinic / hospital immediately.

If you feel you can no longer manage the situation at home, you must always come to the treating clinic / hospital with your child.

3.5 Are there new therapy options for the dietary management of fatty acid oxidation disorders?

Various new therapeutic approaches are being studied, but they are still not used in the standard care of patients. New therapies must be tested for all possible outcomes before being used in as a main therapy option.

At present, the C7 fatty acid triheptanoin has been given instead of the usual MCT fats. Triheptanoin, fatty acids are made available to the metabolism and can avoid the defective metabolic pathways thus serving as an alternative energy source.

Due to its particular composition, triheptanoin is broken down to so-called ketones which can be used for energy production in the body. The studies showed an improvement in heart function. Ketones are already “finely cut” fatty acids. They are being tested as an alternative energy source for patients with fatty acid oxidation disorders.

Some substances are also being tested which may lead to an increase in enzyme activity (bezafibrate, resveratrol).

3.6 How is the dietary therapy carried out?

The diet is based on the recommendations for healthy, age-appropriate nutrition from the German Research Institute of Child Nutrition (Forschungsinstitut für Kinderernährung, FKE). However, these recommendations must be adapted to the specified requirements of the individual therapy (see chapter “What does daily therapy look like”).

The adaptation comprises the following aspects:

- Regular meals
- Sufficient energy intake
- Low-fat range of foods to reduce long-chain fatty acids in the diet
- Use of MCT fat to cover the energy demand
- Dose of essential fatty acids to counterbalance their deficiency in a low-fat diet
- Adjustment of the child’s diet to the family’s diet

The therapy is individually adjusted according to the type and severity of the enzyme deficiency. Therapies can roughly be divided into a “moderate” and a “strict” diet. But there are also variations in between based on the individual. Your metabolic team therefore gives you precise recommendations for the therapy of your child. In some children, regular meals are sufficient, whereas other patients need a very strict low-fat diet.

3.6.1 Why are regular meals important?

An important element of the therapy is the avoidance of so-called **catabolic metabolic situations (catabolism) also known as “metabolic crisis”**. These are situations in which the body must rely on its reserves, paricularly its fat reserves. The main reasons for this are an increased energy demand or a reduced energy intake.

Reasons for catabolic metabolic situations with an increased energy demand:

- Fever
- Infections
- Vaccinations
- Operations
- Teething
- Sport, physical strain

Reasons for catabolic metabolic situations with a reduced energy intake:

- Loss of appetite, e.g. in case of heat, if food has no taste, illness
- Long periods of fasting i.e. a long time between meals
- Abstention from high-calorie foods
- Forgetting / missing meals
- Gastro-intestinal infections with vomiting and diarrhoea
- Deliberate calorie reduction (“weight loss diet”)

The body first always relies on its sugar reserves (stored carbohydrate). Sugar reserves are stored as glycogen in the liver and in the muscle. These reserves are used relatively quickly, so that the body must rely on the fat stores. The body’s own fat stores consist of long-chain fatty acids which are broken down in beta oxidation in the same way as food fat. When there is an enzyme deficiency in beta oxidation, little or no energy at all can be produced from body fat. Regular and sufficient supply of non-fat energy through food is therefore particularly significant, and must always be guaranteed.

The smaller the child, the quicker the sugar reserves are used. Infants and small children must therefore eat and drink significantly more often than school children, young people and adults. It is also important to pay attention to fasting periods at night. Due to rest, the body needs less energy at night than during the day, but it still relies on a sufficient energy provision.
The table below provides an overview of how long the times between meals should be. It is crucial that the patient eats sufficiently during the day so that energy reserves are full. If this is not the case or if the patient has fever or an illness, then the time period between meals should be shortened both during the day and at night.

Recommended maximum time period between two meals based on age groups:

Important: The information applies only if the child has no infection and has eaten enough during the day! These are general recommendations, your metabolic team’s recommendations for your child may vary.

Age	Daytime	Night
Newborns	3 hours	3 hours
up to 6 months	4 hours	4 hours
6 - 12 months	4 hours	6 hours
1- 3 years	4 hours	8 hours
from 4 years	4 hours	10-12 hours

3.6.2 How strict must fat restriction be in the diet?

The required fat restriction is individually determined for each patient. A mild, moderate or strict fat reduction is recommended depending on the type and form of the enzyme defect. But there are also varations in between.

Moderate fat restriction

Many foods are naturally low infat. These include, apart from a few exceptions, fruit and vegetables, pulses, potatoes, cereals and drinks. As long as the fat content of these foods is not increased through processing (so-called hidden fats), these can be eaten without limitation. A good example of “hidden fats” is potatoes: potatoes themselves have no fat. They can be used to make boiled potatoes, jacket potatoes or dumplings. When prepared and eaten as fried potatoes, chips or crisps, a large amount of fat is added to them, which is absorbed by the potatoes and therefore also eaten and therefore not suitable for a fat restricted diet.

Foods very rich in fat such as butter, cream, bacon, very oily or chocolate should not be eaten. In foods containing fat such as meat, fish, sausages, milk, cheese, ready-made products and sweets, the fat content is reduced in the diet by choosing suitable products. Many of these foods can be eaten in low-fat variants. For example, whole milk with 3.5 % fat can be replaced with semi skimmed milk with 1.5 % fat.

By restricting the quantity of fat, the diet is also lower in calories. The deficit is met using MCT fat. Upon consultation with your treatment team, MCT fat is used in varying quantities in your daily diet. Furthermore, the intake / supplmentation of essential fatty acids must be considered.

Strict fat reduction

This therapy builds upon the moderate therapy however foods containing fat are even more restricted. Just like in the moderate therapy, all foods which are naturally low-fat can be consumed without limitation. However, the patient relies on the very low-fat variants of foods containing fat.

Whole milk with 3.5 % fat is replaced by skimmed milk with 0.3 % fat. Regarding meat, fillets, tartare or skinless chicken can be eaten. Within a strict fat reduction, the use of MCT fat is a necessary complementary component of the therapy. MCT fat supplies important energy which can be used by the body without any subsequent fatty acid build-up. The precise quantities for your child are determined by the treating metabolic team. The dietitian / nutritionist will check the intake of essential fatty acids and recommend suitable products as required.

3.6.3 How can fat be reduced in the diet?

A simple way of consuming less fat is to remove visible fat e.g. the fat strip in meat. Many foods **rich in fat** can be swapped with **low-fat** substitutes, so that they do not have to be given up completely. Other foods such as fruit, vegetables, potatoes or rice are naturally low-fat or fat-free. In packaged foods, the fat content is stated in the nutritional value analysis. This is helpful when choosing products.

A few foods from the family diet must be replaced by alternatives with low fat or **containing MCT**.

Here is a list of options:

High-fat foods	Moderate fat reduction	Strict fat reduction
Whole milk 3.5 % fat	Semi-skimmed milk 1.5 % fat	Skimmed milk 0.3 % fat
Mascarpone Cream curd cheese 40 % fat Curd cheese 20 % fat	Curd cheese with 10 % fat, Low-fat curd cheese	Low-fat curd cheese
Cream yoghurt 10 % fat, Greek yoghurt Yoghurt 3.5 % fat	Yoghurt 1.5% fat	Yoghurt 0.3 % fat
Cream 30 % fat	Soy cream light, sour cream Concentrated milk 4 % fat Yoghurt 1.5 % fat	Small amounts of sour cream Concentrated milk 4 % fat Yoghurt 0.3 % fat
Double cream Crème fraîche Smetana (sour cream)	Sour cream	Small amounts of sour cream Yoghurt 0.3 % fat
Cheese > 45 % fat in dry matter	Cheese up to 30 % fat in dry matter	Cheese up to 10 % fat in dry matter
Double cream cheese	Cream cheese < 15 g fat / 100 g	Cream cheese < 5 g fat / 100 g low-fat curd cheese
Eggs	Egg white Replace eggs in baking with apple sauce, banana, baking soda with vinegar	Egg white Replace eggs in baking with apple sauce, banana, baking soda with vinegar
Salmon	Low-fat fish, e.g. cod or tuna in brine or water	Low-fat fish, e.g. cod or tuna in brine or water
Pork mince Mixed minced meat	Minced beef	Tartare
Bacon	Low-fat bacon (diced)	Boiled ham, rolled fillet of ham
Raw ham	Boiled ham, rolled fillet of ham	Boiled ham, rolled fillet of ham

High-fat foods	Moderate fat reduction	Strict fat reduction
Salami	Low-fat salami Salami light	Corned beef (no fat)
Mayonnaise	Kanso DeliMCT Cream	Kanso DeliMCT Cream
Hazelnut spread	Jam, marmalade, jelly, honey	Jam, marmalade, jelly, honey
Potato crisps	Crackers light	Salt sticks, pretzels
Chocolate	Gummy bears, lollipops	Gummy bears, lollipops
Dairy ice cream	Fruit ice cream	Sorbet, ice lolly
Butter biscuits	Russian bread (alphabet biscuits)	Russian bread (alphabet biscuits)
Butter, margarine	Kanso MCT margarine 83 % Half-fat margarine Tomato paste, mustard	Kanso MCT margarine 83 % Tomato paste, mustard
Vegetable oils	MCT oil	MCT oil
Cream cake, butter cream cake	Sponge flan, yeast dough, meringue Cake baked with MCT fat	Sponge flan, yeast dough, meringue Cake baked with MCT fat
Puff pastry	Strudel pastry yufka dough	Strudel pastry yufka dough
Chips	Oven chips Chips from the hot air fryer (no added fat)	Oven chips Chips from the hot air fryer (no added fat)
Mashed potatoes	Spray semi-skimmed milk with Kanso MCT margarine 83 % on a baking tray and bake the mashed potatoes in the oven use to scallop casseroles	Spray skimmed milk with Kanso MCT margarine 83 % on a baking tray and bake the mashed potatoes in the oven use to scallop casseroles

3.6.4 How can dishes be prepared in a low-fat manner?

You can consume less fat with suitable preparation methods or suitable cooking equipment, but also tricks in the preparation or recipe alterations help reduce the fat content.

Frying, cooking, boiling:

- Grease the pan with oil and then sauté
- Cook in a clay pot (soak, fill with the ingredients and place in the cold (!) oven, heat up the oven)
- Prepare / cook in an oven bag
- Cook the ingredients in the oven and grill to brown
- Boiling, stewing, steaming and grilling are low-fat preparation methods

Baking, low-fat pastries:

- Cake batter: Reduce the amount of egg, use very carbonated mineral water, replace the egg with apple sauce or banana
- Shortcrust pastry: prepare with Kanso MCT margarine 83 %, leave out or reduce egg
- Yeast dough: make without egg
- Curd cheese-oil dough: make with MCT oil
- Try out vegan recipes (caution with tofu, soy flour, almond butter or egg substitute! They are rich in fat)

Egg alternatives:

- 1 egg = 80 g apple sauce (can replace up to 3 eggs)
- 1 egg = ½ ripe banana (can replace up to 3 eggs)
- 1 egg = 80 g pumpkin sauce (can replace up to 3 eggs)
- 1 egg = 1 tbsp mild vinegar + 1tsp baking soda or baking powder
- Very carbonated mineral water loosens the dough
- Tomato paste or low-fat curd cheese can be used for binding in meatballs
- Turmeric dies the pastries yellow

Sauces:

- Replace roux with puréed vegetables or with flour mixed with water
- Replace cream with concentrated milk 4 % fat
- Prepare salad sauces with MCT oil, yoghurt or buttermilk
- Prepare sauces for pasta or vegetables with low-fat cream cheese, vegetables, puréed vegetables

Dessert:

- Cook pudding, semolina pudding, rice pudding with semi-skimmed / skimmed milk
- Use low-fat / skimmed yoghurt, buttermilk or curd cheese for creams
- Make ice cream with frozen fruits
- Refine fruit salads with walnuts (essential fatty acids)
- Make tiramisu by using honey cakes with low-fat curd cheese and fruit

3.6.5 What is MCT fat and how can it be used?

MCT fats are medium-chain fatty acids. These fatty acids can be used as an energy source by people with a disorder in the breakdown of long-chain fatty acids. Another enzyme is active here which facilitates the breakdown of the medium-chain fatty acid. This also creates energy. For this reason, MCT fats are specifically used in the therapy of disorders in the oxidation of long-chain fatty acids. MCT fats are an energy source which can be metabolised very well especially in muscle cells. MCT fat can be taken before physical strain to provide the intensely working muscle cells with sufficient energy. In rest periods, e.g. during the night, MCT fats are not normally needed. In the daily diet, MCT fat counterbalances the calorie deficit from low-fat foods. The respective quantity is determined individually by the dietary team. MCT fat should be used as to meet and not exceed energy requirements, as too much MCT fat is also stored as body fat. When stored as body fat, excess fat is converted into long-chain fatty acids therfore no longer available as an energy source.

The special medical foods industry provides various MCT products specifically designed for patient with disorders of fatty acid metablisom. There is MCT oil with varying MCT fat content. MCT margarine to replace butter or vegetable margarine. MCT powder that can be mixed in food and drinks. There is special MCT baby formula for infants, where long-chain fatty acids are largely replaced by MCT fat. MCT baby food supplements breast milk or “normal” baby food. Babies in strict therapy are exclusively fed MCT baby food. The nutritional profile of MCT baby food is based, like any other baby food, on the composition of breast milk.

Pure MCT fat has a lower smoke or melting point then other fats. It should therefore not be heated too much. MCT oils can be used after cooking to lightly sauté or used in cold dishes It should therefore be used for cooking as briefly as possible and at medium temperatures. The MCT margarine and the oils can be used for baking. MCT products such as Kanso MCT margarine 83 % are available on prescription.

3.6.6 What is the significance of essential fatty acids?

Essential fatty acids are vital for the body. However, the body cannot produce them itself, so they must be eaten with food. They belong to the group of the so-called omega fatty acids.

For example, the Alpha linolenic acid (ALA), also called linolenic acid, is one of these omega-3 fatty acids. From this, the body can produce two other omega-3 fatty acids: docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). They have an have an anti-inflammatory effect and are cell components. For instance, DHA is found in large quantities in the nerve cells of the brain and in the retina of the eye. EPA is the precursor of DHA and eicosanoid, which are also important for the immune system, blood coagulation and the regulation of blood pressure.

Linolenic acid is found in large quantities e.g. in linseed oil. But also walnut, rapeseed and soy bean oil are good sources of linolenic acid. Oily fish such as salmon or herring contain DHA and EPA. Microalgae, the food sources of fish, produce these fatty acids. Omega-6 fatty acids are another important group of essential fatty acids. Linoleic acid and arachidonic acid are two examples of omega-6 fatty acids. Linoleic acid is an integral part of skin cells. With a low-fat range of foods, an insufficient amount of essential fatty acids is consumed. For this reason, a defined amount of these fatty acids must be ingested regularly. The required amount is individually determined for each patient by the dietary team. Walnut, linseed or soy bean oil are good suppliers of essential fatty acids. DHA is available in capsules.

3.6.7 What should you bear in mind in case of illness and infection?

An **emergency therapy** must be carried out in case of fever inducing infections, refusal of food or long periods of fasting, e.g. before operations.

If your child wants to eat during an infection, he or she is allowed to do so. In the event of an infection, a stricter fat reduction in the diet is not necessary. However, in case of an infection, it is particularly important to observe the recommendations regarding the maximum intervals between meals.
If your child has an infection / illness and does not want to eat much or at all, you can carry out an emergency therapy at home, which can often avoid an inpatient admission. Large amounts of carbohydrates must then be given through drinks (e.g. with the intake of a maltodextrin solution, tea / water with sugar).

The amount of carbohydrate required depends on the age and weight of the patient and is individually calculated by your metabolic treatment team.

3.6.8 What does the diet consist of in the first year of life?

In the first few months of life, a child's diet changes constantly. This is also the case for children with disorders in long-chain fatty acid oxidation. The diet is based on the recommendations for children without metabolic disorders, but it is adapted to the respective requirements of the metabolic disorder.

In the first few months, the infant drinks **breast milk** or **MCT baby food**. They can also be combined to ensure optimal growth and reduce long term complications.

Between the ages of 4-6 months, milk meals are gradually replaced by weaning foods. The first weaning foods consists of vegetables, potatoes and low-fat meat. The second stage of weaning can begin after 6 months of age and includes milk and cereals..During the course of weaning, the food becomes increasingly lumpy and, at the end of the 1st year of age, the child can eat with the family. The child's meals are then adapted to the family meals depending on the severity of the fat restriction, example of diet adaption in the first year of life are detailed below:

Diet adaptation in the first year of life

Age	Food	Moderate fat reduction	Strict fat reduction
0 – 6 months	Breast milk or baby formula (preterm formula)	Breast milk MCT baby formula	MCT baby formula
5. – 6. month	Breast milk or baby formula (Pre-formula) Vegetable, Potato, Meat and Porridge & rapeseed oil	Breast milk & MCT Baby formula Vegetable-potato-porridge with low-fat meat & MCT oil	MCT Baby formula Vegetable-potato-porridge with low-fat meat & MCT oil 100 %
6 – 7. month	Breast milk or baby formula (Pre-formula) Vegetable-Potato-Meat-Porridge & Rapeseed oil Milk-cereal-porridge	Breast milk & MCT Baby formula Vegetable-potato-porridge with low-fat meat & MCT oil Milk-grain-porridge with low-fat milk	MCT Baby formula Vegetable-potato-porridge with low-fat meat & MCT oil 100 % Milk-grain-porridge with skimmed milk or MCT Baby Food
7. – 8. month	Breast milk or baby formula (Pre-formula) Vegetable-Potato-Meat-Porridge& rapeseed oil Milk-cereal-porridge Fruit-Grain-porrige	Breast milk & MCT Baby formula Vegetable-potato-porridge with low-fat meat & MCT oil Milk-grain-porridge with skim milk Fruit-Grain-Porrige	MCT Baby formula Vegetable-potato-porridge with low-fat meat & MCT oil 100 % Milk-grain-porridge with skimmed milk or MCT Baby Food Fruit-Grain-Porridge
10. month onward	Solid food from family food replaces the porridges	Bread meal with MCT margarine or flakes with low-fat milk Snack of fruit, vegetables, Yoghurt, bread / toast Warm Meal & MCT Fat Snack of fruit, vegetables, yoghurt, pastries, bread / toast	Bread meal with MCT margarine or flakes with skimmed milk & MCT fat Snack of fruit, vegetables, yoghurt, bread / toast & MCT Fat Warm Meal & MCT Fat Snack of fruit, vegetables, yoghurt, biscuits, bread / toast & MCT fat

Vegetable, potato and meat pap

1 carrot
100 g

1 potato
50 g

1 tbsp minced meat 25 g

3 tbsp fruit juice
30 ml

1 tsp MCT oil
5 g

Preparation:

1. Peel the carrot and potato and cut into small pieces.

2. Cook the carrot and the potato in a pot with a little water.

3. Cook the minced meat in a pan with MCT oil.

4. Purée the carrot, potato and tartare with oil and fruit juice.

1 parsnip
100 g

1 potato 50 g

2 tbsp Hipp meat 30 g

3 tbsp fruit juice
30 ml

1 tsp MCT oil
5 g

Preparation:

1. Peel the parsnip and potato and cut into small pieces.

2. Cook the parsnip and the potato in a pot with a little water.

3. Purée the parsnip, potato, Hipp meat, MCT oil and fruit juice.

Milk and cereal pap

1 glass of milk
200 ml*

2 tbsp cereal flakes 20 g

1 tbsp fruit purée
20 g

* (skimmed / semi-skimmed milk depending on fat restriction)

Preparation:

1. Heat up the milk in a saucepan.

2. Stir in the cereal flakes.

3. Leave to cool.

4. Stir in the fruit purée.

6 MS MCT food
See packaging

1 glass of water
180 ml

2 tbsp dairy-free cereal pap
See packaging

2 tbsp fruit juice
20 g

MS = measuring spoons

Preparation:

1. Bring the water to the boil and leave to cool.

2. Stir the milk powder and cereal pap powder into the water.

3. Stir in the fruit juice.

Fruit and cereal pap

2 tbsp cereal flakes 20 g

½ glass of water 100 ml

5 tbsp fruit purée 100 g

1 tsp MCT oil 5 g

Preparation:

1. Bring the water to the boil and leave to cool.

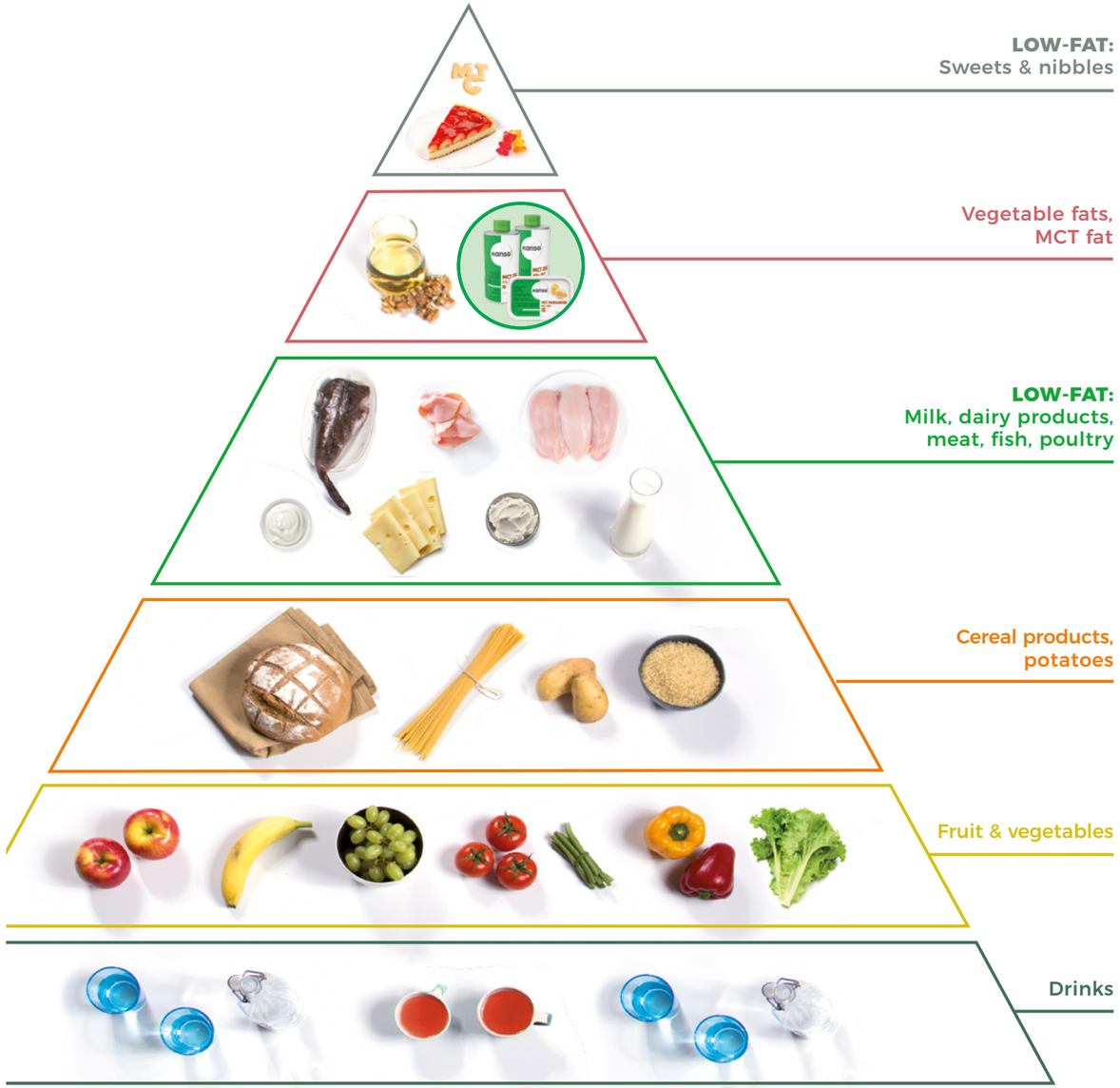
2. Stir in the cereal flakes.

3. Stir in the fruit purée and the MCT oil.

3.6.9 How can the child's meals be adapted to the family's meals?

At the end of the first year of life, a child's diet resembles the family diet more and more. Meals have a more solid consistency and the range of individual foods and dishes has expanded.

The **food pyramid** illustrates the composition of the daily diet of a child with a disorder in the metabolism of long-chain fatty acids. Much of it resembles the recommendations for a healthy, varied diet of children with a healthy metabolism. Sufficiently sugar-free drinks such as mineral water, fruit tea and small amounts of fruit juice mixed with sparkling water are important. Fruit and vegetables have a high priority. These are fat-free and can be eaten in unlimited quantities. It is recommended, like it is to everyone, to eat 5 portions of fruit and vegetables a day. A portion corresponds to the consumer's fist size or to the amount that fits into cupped hands. The next level of the food pyramid contains cereal products and potatoes. These should be prepared in a low-fat way. Low-fat milk and dairy products enrich the daily diet and are supplemented by smaller amounts of low-fat meat and sausage varieties. Oils and spreadable fat must be replaced with MCT fat and enriched with essential fatty-acids depending on the therapy. Sweets and snacks form the tip of the pyramid.



3.6.10 How can a fat-modified diet be implemented into a child's varied everyday life?

Nursery / school attendance, birthdays and trips

Food with the childminder, at the nursery / school, etc.

1. Information for carers, educators and teachers on the metabolic disorder given by the parents or the metabolic team. The following themes can be discussed here:
- What disorder does the child have?
- What emergencies can occur and what should be done?
- What can the child eat and what can he or she not eat?
- What do meals together look like?
- What happens when the child has eaten something unsuitable?
- Who should be called in case of any questions?

2. Discuss the breakfast buffet, choose suitable foods together and, if required, supplement with dishes brought from home
3. Check the meal plan and choose the suitable choices using recipes available. If required, supplement lunches with homemade dishes brought from home. Clarify with the caterer whether "special meals" can be ordered
4. Stock up on suitable and storable foods in the facility.
5. Advance information by the parents on birthdays, trips, parties. So that e.g. a suitable cake can be provided
6. Inform the carer that it is unlikely that anything severe will happen. A single diet mistake does not have any severe consequences. But the therapy is still important!
7. Provide a phone number for emergency cases and inquiries

Children's birthdays, family celebrations...:

1. Discuss with the family hosting the event what there is to eat
2. Bring along a cake, muffins etc.
3. Give tips for baking with MCT fat
4. Inform the hosts that it is unlikely that anything severe will happen
5. Make suggestions for foods and dishes that all children can eat

- Gummy bears, fruit gums, lollipops, savoury snacks, alphabet biscuits
- Pasta with tomato sauce / bolognese with minced beef; pizza with boiled ham / tuna in its own sauce / low-fat grated cheese;
- vegetables; filled jacket potatoes; pancakes; pasta salad

(For sample recipes, see brochure "Nutrition and diet therapy in beta oxidation disorders of long-chain fatty acids")

Cinema, bike tour, swimming pool, walking tour...:

1. Cinema: Fruit gums, liquorice, wine gums, sweets, slushies, ice lollies, fruit ice cream
2. Bike tour: Bring sufficient food along, plan regular small snacks, bring MCT fat for the physical strain, look out for symptoms such as muscle pain and plan breaks
3. Swimming pool: Bring along MCT fat for the physical strain, look out for symptoms such as muscle pain (use MCT if necessary), at the kiosk you can buy ice lollies, slushies, fruit gums
4. Walking tour: bring along / supply sufficient suitable food, inform carers on the necessity of regular meals
5. Provide a phone number for inquiries and emergency cases

Restaurant, fast food, ice cream parlour:

1. Restaurant: Salad without dressing (but vinegar, salt, pepper), soups (no cream soup), pasta with tomato sauce or vegetables, low-fat fish, steak, potatoes, vegetables without sauce / butter, pizza with vegetables / boiled ham without cheese
2. Fast food: Wrap with vegetables, chicken, salad, sushi with low-fat fish, bread roll, sandwich without tartar sauce / butter with boiled ham, turkey breast, smoothie
3. Ice cream parlour: Fruit ice cream, sorbet in a cup with sugar sprinkles

Staying the night with grandma and grandpa, relatives and friends...:

1. Inform them about what your child can and cannot eat
2. Advise on regular meals and ensuring that long periods of fasting should be avoided
3. Discuss night breaks and a late meal / night meal if required
4. Supply MCT fat
5. Supply food, a late meal / night meal if required
6. Provide a phone number for enquiries and emergency cases

Staying the night in a nursery school, youth hostel...:

1. Inform them about what your child can and cannot eat
2. Advise of regular meals and ensuring that long periods of fasting should be avoided
3. Discuss maximum night breaks and a late meal / night meal if required
4. Supply MCT fat and clarify the possibility of refrigerating
5. Supply food, a late meal / night meal if required
6. In case of physical strain e.g. hiking, look out for possible symptoms such as muscle pain. Pay attention to the intake of MCT fat
7. In case of day trips, make sure the child has enough to eat and drink
8. Provide a phone number for enquiries and emergency cases

Attached you will find an information leaflet for carers (nursery school, educators, teachers). This provides a brief summary of the most important information on the clinical picture and on the therapy.

4 Developmental psychology section Information for families with a chronically ill child in the infant and preschool age - The period from birth to the sixth year of life

4.1 Do you need any special parenting skills or parenting techniques if a child has a fatty acid oxidation disorder?

After the diagnosis, you are likely to feel overwhelmed at first by all the information you have been given. Many words you didn't know until now have been used to explain your child's situation. You have probably never heard of disorders of fatty acid oxidation, and you are wondering what this means for you and your child: Is the disorder dangerous (or life-threatening)? What should I expect? Is there a dietary management or even a cure? Why does my child, of all people, have this metabolic disorder? You soon learn what the dietary management is like and to which results it can lead, but you have no doubt wondered whether you can handle the situation with what you know so far and with the resources you have available.

Some parents think you need special parenting techniques to bring up a child with a metabolic disorder. But this is not the case. Along with a somewhat deeper knowledge of foods and nutrients, there are only a couple of additional considerations (rules of conduct) when raising a child with a fatty acid oxidation disorder.

With the support of your metabolic team, knowledge about foods can be acquired easily and quickly. The rules of conduct are easy and not that different from the rules that parents should follow when feeding and bringing up a child.
Before these are explained in individual examples, the most important characteristics of disorders in the metabolism of long-chain fatty acids and their dietary management should first be repeated one more time.

4.2 What are the six most important characteristics of fatty acid oxidation disorders and their dietary management?

1. The body's capacity to gain energy from long-chain fatty acids is restricted.
2. In the following situations, this can lead to dangerous low blood sugar (hypoglycaemia) or to damage in the body:
- Long breaks between meals or refusal of food
- Increased physical activity (including sport)
- Fever inducing infections / illness including vomiting, diarrhoea
- Operations / surgery

3. Energy deficiency can damage the brain, liver, heart muscle and the skeletal muscles, and in some cases can even lead to life-threatening situations and even death.
4. You can counteract the specific problems in metabolic disorders of long-chain fatty acids with:
- Regular meals
- Preventive eating or precaution in case of planned physical strain (e.g. sport, operations)
- Dietary measures, i.e. avoiding long-chain fatty acids, use of medium-chain fatty acids (MCT fats) instead.

5. The metabolic disorder can take various forms. There are severe and moderate forms which require strict and less strict dietary management measures. Moderate forms can also become dangerous in situations with great energy deficiency (very long breaks between meals) or high energy consumption (extreme physical effort, illness). This also includes operations, as you are not allowed to or cannot eat before, during or after a general anesthetic and operation; you also have an increased energy requirement due to the operation itself.

4.3 The period from birth to the sixth year of life

The first six years of a person's life are extremely important, but also eventful and varied. A person never stops learning, but, in this period, children probably learn more than they ever will in the rest of their life. At any rate, a child learns many things which he or she then later perfects mainly with practice.

These include, for example, the following skills:

- How to swallow solid food and how to drink from a cup.
- How to sit, stand, walk and run while keeping one's balance. How to go up the stairs and climb. How to reach for objects which used to be out of reach, but can also put themselves at risk.
- How to use and control individual body parts. How to grab, hold or move something e.g. with hands and fingers: a pen when drawing, a spoon when eating, a toothbrush when brushing one's teeth. Toilet training (first during the day and later also at night).
- At around one year of age, children learn to specifically pronounce individual words; they then add a new word almost every day and, from their second birthday, children learn several new words daily.
- Being able to notice things, look at them carefully and differentiate them (e.g. who is mum, dad, what are the siblings' names, pets and foods called?). Not everything that has four legs is a dog, and you should not touch everything that looks interesting: for example stinging nettles or a hot oven. Not everything that is called meat contains the same amount of fat.
- An extremely important skill for learning is to be able to listen. Of course, every person must eat and drink on their own, climb stairs, scribble with a pen, learn the names of colours and where to find the playground. However, instructions are very helpful. Without instructions, much learning progress would need at least a lot more time, and some would be linked to pain or even dangerous. Touching a stinging nettle is painful, but not dangerous. If each person had to find out on their own that you cannot simply run across the road, this strategy would be frequently linked to death and therefore also to the end of each learning progress. This is also the case for nutrition. You can eat or drink some things, while others you cannot ingest at all. Listening is therefore very helpful when learning what something is called, how something works, what one does when and how one should or should not do or is not allowed to do. As a result, it is also very important for children if people they listen to know something well and are well informed on how children learn.

4.4 In all development phases, parents can choose from a great range of food options

Raising children always brings up two questions.

The **first** question is: What are children **allowed** to do when, how often, with whom or alone?

The **second** is: What **should** children do when, how often, with whom or alone?

Just as parents choose what toys to give their child, they also choose what children eat and decide when they eat. Of course, children may and should also have preferences and express wishes, but it is ultimately the parents who give the children leeway. This applies to the range of foods as well as the mealtimes. It is therefore important to start very early to accustom the child to a fixed rhythm.

4.4.1 What parents and educators of children with an oxidation disorder of long-chain fatty acids should know about nutrition and the metabolism.

A functioning metabolism of long-chain fatty acids relieves us of two important decisions:

Firstly, we don't need to think about which foods we want to choose from the customary range.

Secondly, we can go without eating for prolonged periods of time, e.g. if we are ill and have no appetite, if we have forgotten to buy something or if we don't eat something deliberately because we want to lose weight.
In fact, to avoid illness, all people and therefore also children should eat in a balanced and age-appropriate manner, and not eat too much or too little; in case of a long-chain fatty acid oxidation disorder, however, one should know more about and consider two things in particular which go beyond common knowledge.

What you need to know

Firstly, one should be more informed about food components, as this is normally the case with conscious nutrition. Furthermore, many doctors and nutrition specialists do not have this specialist knowledge, which is why you are assigned to a metabolic centre.

Secondly, you should learn in more detail how the body's energy balance functions, the role different nutrients have and how the body works between meals. Especially what role the period between meals plays and what it means to fast.

Conclusion: Parents of a child with an oxidation disorder of long-chain fatty acids, like all parents, should be well informed about an age-appropriate and balanced diet and the significance of regular meals, but in greater detail.

4.4.2 What parents and educators of children with a disorder in the metabolism of long-chain fatty acids should know about children's development.

Children grow very quickly in their first year of life. This means that, with the energy and nutrients from their diet, they build body massvery quickly. Children's nutrition must therefore be constantly adapted to their age and activity level, so that they can grow and thrive correctly. As newborns can only ingest relatively small amounts of food and consume the energy it contains rapidly, they quickly become hungry (which newborns communicate by crying). They must therefore be fed frequently: at the beginning every three to four hours, including night time too, but the night sleeping phases become longer and longer.

Conclusion: Parents of a child with an oxidation disorder of long-chain fatty acids, like all parents, should be well informed about the child's natural eating rhythm and its significance for growth, but in greater detail. Along with the child's drinking rhythm, the specifications on the maximum age-appropriate intervals between meals must also be considered in the diet.

In case of vomiting or diarrhoea, not only do we lose the energy supplied to the body, but we also often lose appetite, i.e. further intake of energy is also reduced or even completely suspended for a considerable amount of time. The body then consumes stored energy (particularly from the stored fat), which is why ill people usually lose weight. Due to their low weight, children only have small reserves (stored energy) and lose weight very quickly when they're ill, which could become dangerous. For this reason, even children without a fatty acid oxidation disorder should see a doctor in case of vomiting, diarrhoea and rapid weight loss, and sometimes also be managed with an infusion.

Conclusion: Parents of a child with an oxidation disorder of long-chain fatty acids, like all parents, should be well informed about the significance of nutrition in case of illness, but in greater detail.

In the first 4-6 months of their life, children are either exclusively breastfed, fed with formula or with a combination of both. For children with fatty acid oxidation disorders there are special formulas which do not appear any different from common baby formulas, but which are very different in terms of their composition. Some children can also be breastfed. Your metabolic team will support you with your choice of bottle feed and with its adaptation to your child's age.

Conclusion: Parents of a child with an oxidation disorder of long-chain fatty acids, like all parents, should be well informed about baby formulas, **but in greater detail.**

Summary: With the diagnosis of a fatty acid oxidation disorder, you are given a lot of information and you will have many questions. However, consider that - at least in terms of nutrition - you now have 4-6 months to calmly learn what your child's meals should consist of and how you must prepare them. Your metabolic team will provide you with systematic and regular support with this.

4.4.3 Are children with a fatty acid oxidation disorder sick?

If your child has a fatty acid oxidation disorder, he or she is not necessarily sick. Of course, your child is sick if he or she has a fever, diarrhoea and vomiting, but then everyone is sick in this case.

If your child was diagnosed at an early stage, e.g. in the newborn screening, and the treatment was started in quickly , this can prevent consequences of the illness from arising. The treatment is then prophylactic (preventive) and preserves the health, i.e. prevents the child from long term complication of the disorder.

Unfortunately, this is not completely true for all fatty acid oxidation disorders covered in this brochure or for all degrees of severity.

Generally speaking, fatty acid oxidation disorders, especially all severe forms, can become dangerous or even be fatal without dietary management, especially due to threatening hypoglycaemias.

The dietary management of a **VLCAD deficiency** and **CPT I deficiency** is so effective that a child's normal development can be expected.

Unfortunately, a **LCHAD deficiency** and **TFP deficiency** cannot always be managed completely. For this reason, development impairments cannot be prevented.

Severe forms of a CPT II deficiency lead to heart, liver and kidney dysfunctions even with a strict dietary management.

Unfortunately, a **severe CACT deficiency** always has a serious clinical course, and a shortened life expectancy must be taken into account.

All moderate or mild forms have no complete enzyme deficiency, but the function of the enzyme is limited. For this reason, the expected course of the illness is usually better. Your metabolic team will therefore discuss your child's individual situation in detail with you.

Conclusion: Try not to regard your child only as sick in everyday life. Don't say "my child is sick", but say "he / she has a metabolic disorder". Don't think "a fatty acid oxidation disorder is **impossible** to deal with", but think about **how you can deal with it despite** the disorder. Discuss your ideas also with your metabolic team, to make sure that you haven't missed anything.

4.5 Behaviour in special situations

What happens in case of a singular or partial deviation from the dietary management recommendations?

What happens if the child has slept half an hour longer than recommended? What happens if the child eats a portion of a standard product instead of "his / her special or diet product"? Discuss these questions early on with your dietary team, so that you yourself can learn what consequences deviations from the recommendation can have. Relatives, friends and other potential carers will no doubt also ask you these questions, and you should be able to answer them with confidence.

Children's birthdays

If your child is invited to a children's birthday party, you should arrange the situation with the birthday child's parents in advance. Other families won't normally have any special products available. Instead, you could provide the birthday child's parents with diet products in advance. Children are very tolerant in terms of differences, provided that each child receives something "of his / her own". At preschool age, being with other children and playing together is far more important that the ingredients of a birthday cake. However, explain to the host parents what would - not! - happen in case of a small diet transgression.

Staying the night with relatives and friends

Relatives will usually first experience the child's disorder together with the parents and learn what to look out for, but also what is allowed. As long as the host parents are informed and prepared to let the child with a metabolic disorder stay with them, the food supply is organised and the parents' house is not too far, a child with a fatty acid oxidation disorder can stay with his or her friends like any other child.

Nursery / school

Children with a fatty acid oxidation disorder should also go to nursery / school like other children. Inform the nursery / school staff about the metabolic disorder and its treatment. If it is ensured that the nursery / school can reach the parents at any time, this will reassure both sides. Whenfood is handed out in the nursery / school, arrangements and preparations must be made. It is not always possible for the nursery / school to have special products available and to prepare special meals for a child with a metabolic disorder. However, even the "normal" meal plan of a nursery / school provides some options. The difference between your child and other children is the planning. For instance, you could prepare the food for your child. Storable "dry" foods such as crispbread / gummy bears etc. should be well-stocked in the nursery / school. You can often store MCT fat in the fridge. It is sometimes helpful if the nursery school can speak directly to the metabolic centre.

Going to restaurants and eating out

Despite a strict avoidance of long-chain fatty acids, it is possible to go to restaurants and eat out. Usually, there is always something your child can eat (see chapter 3.6.10)! Perhaps you can bring along dishes and ask to heat them up in the kitchen, or you can bring an MCT salad sauce and ask to use this for your child's salad. For your "local restaurant", you should discuss this in advance with the kitchen in due time. Sometimes chefs are even happy to take on this special task. Many chefs can now adapt dishes off the cuff. Parents must dare to ask.

4.6 How do you introduce your child to the diagnosis and the diet?

What should the child know?

In the first six years of their life, children usually do not make any decisions on their own on what or when they are going to eat. However, children should learn from an early age that there are special foods for them, e.g. that they can say "my sausage, my food". Children at preschool age are very tolerant when it comes to differences, and are often even proud of them. Children also drink fruit tea from their own "children's cup" and eat with a spoon, not with a knife and fork. As parents, you should not perceive these differences as a disadvantage.

What should you explain to your child and how?

Children can only absorb and understand as much as they are able to from their stage of development. Talk to your child about anything related to his or her metabolic disorder in the way you would talk about other important things.

Be careful not to take your child's questions in a more complicated way than they are meant. With the question "Why should I have my own sausage?", the child does not expect a lecture on the metabolism of long-chain fatty acids. At the age of two and three, it is sufficient to generally reply e.g. as follows: "You have your sausage and mummy and daddy have their own sausage; we also drink our tea and your have your own tea. But you must make sure you always eat the right sausage."

At a next stage you can explain that this is important to stay healthy. Avoid telling your child that he or she is sick if they are not actually sick. A good strategy is to say "So that you don't get sick, so that you stay healthy". Like in other educational areas, you can reformulate things that are not permitted into rules easily. It is much more effective to tell your child what they should do instead of what they shouldn't do: "Before crossing then road, you need to look left and right to see if a vehicle is coming" instead of "You are not allowed to just run across the road".

Who should explain things to your child?

If sometimes you are unsure how you should reply to your child's question or how you should react to unwanted behaviour, you can suggest to your child to discuss it with your metabolic team during your next visit to the metabolic centre. Management recommendations are the result of **medical necessity**, while breakfast tea is a familiar **habit** or a preferred taste. When visiting the metabolic centre, your child will see that the parents also have to comply with dietary management orders and that they have not come up with the dietary management measures themselves.

Should the whole family adapt their diet to that of their child?

Even if it was certainly possible for health and practical reasons for the whole family to eat according to the child's diet plan at home, this is not advisable for two reasons.

Firstly, children in their first year of life have a very different diet compared to adults, and, even after that, children and adults often have very different tastes.

Secondly, the child will see in nursery , but in school at the latest, that his or her diet differs from that of other people. Nutrition with a low-fat diet should become a natural characteristic specific to your child as early as possible. This is supported by the fact that a conscious refusal or preference of specific foods is accepted in society and even taken into account in many parts of everyday life. Don't be afraid of natural differences. If you try to compare your family and other families, you will notice many differences which you would like to keep or even hold in high regard.

Rewards

The best reward for a child is praise, and the shared pleasure that something has gone well. All the small steps in the development of the eating behaviour during the first six years of one's life are usually accompanied by praise: biting off bread on your own, drinking from a cup on your own, using a spoon, later a fork and so on. Special rewards are not attached to this for any child. Visits to the clinic, and tests and blood sampling linked to these, do not require a reward either. Cooperation in tests and blood sampling should, if at all, be mainly rewarded by the metabolic team and not by the parents. Mentioning role models can help with the natural urge to copy: "Even athletes have healthy diets and eat before a competition."

5 Explanation of important terms

Acylcarnitines	Acylcarnitines are fatty acid residues linked to carnitine.
Anabolism	This is a situation where the body builds up reserves, i.e. has more energy available than it consumes in the moment. Anabolism is the opposite situation to catabolism (see catabolism).
ß oxidation (i.e. “beta oxidation”)	Breakdown of fatty acids which takes place over several stages.
Blood sugar	Concentration of sugar (more accurately glucose) in the blood.
Carnitine	A substance which is linked to long-chain fatty acids so that they can be transported to their breakdown location. Furthermore, fatty acids linked to carnitine are excreted in the urine.
Dysfunction	(see metabolic crisis)
Enzyme	An enzyme is a substance that supports a special metabolic stage. If an enzyme is missing, the corresponding metabolic stage cannot occur normally.
Fat	Fat is a vital nutrient. The basic chemical structure of all fats is the same: three fatty acids are attached to a portion of glycerine. With the variety of fatty acid chains, different fats are created. Fats form the body’s main energy reserve.
fatty acids	are fat components. A distinction is made, among others, between long-chain and medium-chain fatty acids, which are transported and broken down differently.
Essential fatty acids Essential means necessary	Essential fatty acids are vital for the body, but they cannot be produced by the body itself. They must therefore be ingested with food. Essential fatty acids belong to the group of the so-called omega fatty acids.
Fatty acid oxidation	Breakdown of fatty acids for energy production.
Gene	A gene is a unit in the genome. A gene contains information for a specific component of the body, e.g. for a special enzyme.
Glucose	A monosaccharide; the most well-known form is grape sugar.
Glycogen	Glycogen is the stored form of glucose. It is mainly stored in the liver and in the muscles. Glucose can be released quickly from glycogen when the body needs energy.
Hypoglycaemia	Hypoglycaemia is another word for low blood sugar (see definition).
Catabolism	These are situations in which the body must rely on its reserves. Reasons for this are an increased demand or a reduced intake of energy. The build-up of body reserves, i.e. the opposite situation to catabolism, is called anabolism.
Carbohydrates	Carbohydrates consist of sugar components. If a carbohydrate only has one sugar component, it is called monosaccharide (e.g. grape sugar), if it has two components, it is called disaccharide(e.g. household sugar or cane sugar) etc. Starch is also a carbohydrate.
LCT fat	LCT fats are long-chain fatty acids.
Maltodextrin	A carbohydrate powder with a barely sweet flavour consisting of glucose. It is frequently used for energy enhancement; adding maltodextrin to drinks or dishes significantly increases their energy content. In long-chain fatty acid oxidation disorders, it is recommended to add maltodextrin to drinks e.g. in case of infections in order to prevent a metabolic crisis due to an energy deficiency.
MCT fat	MCT fats are medium-chain fatty acids. These fatty acids can also be used as an energy source by people with a disorder in the breakdown of long-chain fatty acids.
Metabolic crisis / metabolic dysfunction	The metabolism is no longer in balance or is at risk of becoming unbalanced. This happens when the body lacks energy. The metabolic crisis is high when the body has insufficient food intakes, illness and operations. But you can effectively prevent and manage them. Symptoms of a metabolic crisis are tiredness and fatigue, muscle pain and symptoms of low blood sugar (see low blood sugar). A laboratory analysis often shows low blood sugar levels, increased liver and muscle values in the blood, an accumulation of large amounts of long-chain fatty acids in the body and a carnitine deficiency.
Low blood sugar	A concentration (amount) of sugar in the blood which is too low. Low blood sugar is a sign that the body lacks energy. In case of severe low blood sugar, the brain in particular can be permanently damaged. Typical symptoms of low blood sugar are sweating, restlessness, shaking, irritability, ravenous appetite, nausea and tiredness. Seizures and a coma may occur in case of extremely low blood sugars. However, in some instances, hypoglycaemias also occur without any typical symptoms.

6 The MCT range by Kanso

Due to their particular nutritional-physiological characteristics, Kanso MCT products help to improve the quality of life forf people with a disorder in the breakdown of long-chain fatty acids.

Long-chain fatty acids are found in the fat which is generally contained in food.. People with oxidation disorders of long-chain fatty acids or those affected by disorders of carnitine-linked transport of fatty acids via the mitochondrial membrane cannot gain energy from these fatty acids. Both problems can be avoided by using MCT fats.

MCT fat is a usable source of energy in oxidation disorders of long-chain fatty acids!

MCT fats can pass directly through the mitochondrial membrane and be easily and gradually broken down in a shortened manner and completely with the help of other enzymes. Plenty of energy can therefore be gained from them for the heart and skeletal muscles.

Kanso Lipano

- A nutritionally complete, low fat, powdered feed. Can be recommended for use in infants as a sole source of nutrition or as a supplementary feed for children and adults.
- Low in long-chain triglycerides (LCT) and high in medium-chain triglycerides (MCT)
- Contains vitamins, minerals, trace elements

NOTE: Standard 15 % dilution:
15 g Lipano + 90 ml drinking water
= 100 ml ready-to-use drink

Indications

- Disorders in the transport of long-chain fatty acids to the mitochondria
- Carnitine transporter defect
- Oxidation disorders of long-chain fatty acids

Kanso MCT Margarine 83 %

- 83 % MCT fat of the entire fat content
- Contains omega 3 and omega 6 fatty acids
- Supplies vitamin A, D, E, folic acid and B12
- Does not contain any hydrogenated fats
- Ready to eat

NOTE: Suitable for energy supplementation in food and for cooking and baking up to 180 °C and max. 40 minutes

Kanso MCT OIL 77 %

- 77 % MCT fat of the entire fat content
- Contains omega 3 and omega 6 fatty acids
- Supplies vitamin A, D, and E
- Ready to eat

NOTE: Suitable for energy supplementation in food and drinks, and for cooking up to max. 150 °C

Kanso MCT OIL 100 %

- 100 % MCT fat of the entire fat content
- Ideal to enrich food an liquids
- Neutral flavour and odour
- Ready to eat

NOTE: Suitable for energy supplementation in food and drinks, not suitable for cooking

Kanso DeliMCT Champignons

- Contains 28 g MCT fat in 100 g of spread
- Ready to eat
- Hearty and delicious with champignon taste

Kanso DeliMCT Tomato

- Contains 28 g MCT fat in 100 g of spread
- Ready to eat
- Hearty and delicious with tomato taste

Kanso DeliMCT Cream

- Contains 53 g MCT fat in 100 g of cream
- Delicious cream
- Ready to eat

NOTE: Tastes particularly refreshing when served chilled

7 Further information

Surfing the internet

If you search for the term “fatty acid oxidation disorder” on the internet, you will find hundreds of German entries and thousands of English entries. If you stumble upon some information online which does not correspond to what you have been told by your metabolic centre, you should discuss this with your metabolic team, instead of thinking that you have been deprived of something. Generally speaking, when you find new information, you should always ask yourself 3 questions:

1. Is the information relevant to my child’s specific fatty acid oxidation disorder?
2. Is it relevant to the severity degree of my child’s disorder?
3. Is it particularly relevant to my child?

Climb

For people with fatty acid oxidation disorders, there is a self-help group in the German-speaking area for congenital **FettS**äuren**O**xidations**S**törungen Fett-SOS (fatty acid oxidation disorders) (www.fett-sos.com). Self-help groups are very helpful for the exchange of information and experiences related to everyday life with a metabolic disorder or its dietary management. This is an important exchange of information regarding cooking recipes, dealing with authorities and institutes. But they also offer people who are in the same situation the chance to exchange views and learn from each other. For example, parents with a small child can find out how older people with the disorder deal with the challenges of the dietary management.

As fatty acid oxidation disorders are rare, the self-help group promotes the exchange between those affected and mutual support in addressing important issues and coping with everyday challenges. However, when comparing with others, be aware that not all fatty acid oxidation disorders are the same, that there are different degrees of severity in each individual disorder and that not all children are the same but unique.

Other fatty acid oxidation disorders

Fatty acid oxidation disorders (abbreviated FAOD), exist not only for long-chain fatty acids but also for medium-chain fatty acids. In case of disturbances in the degradation of medium chain fatty acids there is a deficiency of the enzyme MCAD „medium-chain acyl-CoA dehydrogenase“.

To avoid confusion, e.g. in diet or fasting times recommendations, it is necessary to separate those with a long-chain FAOD and those with a MCAD deficiency. Affected families can also find related links on the association’s home page (www.fett-sos.com) and an online forum for long-chain FAOD (www.lchad-mtp-vlcad.com) and medium-chain FAOD (www.mcad-infos.de).
Affected families who have a child with a carnitine transporter disorder and must observe a reduced fat diet can also get in touch via the respective websites.

The logo of the website FatAcidsOxidationDisturbances Fat-SOS illustrates this very beautifully. The lack of Trifunctional Protein / TFP deficiency is sometimes also referred to as mitochondrial trifunctional protein, hence the abbreviation MTP.

8 Information for carers of children with disorders in the metabolism of long-chain fatty acids

NAME; SURNAME: .....

Mother’s phone number: ..... (for contact during the day)

Father’s phone number: ..... (for contact during the day)

Name / phone number of another informed contact person:

.....

..... has a congenital disorder in the metabolism of long-chain fatty acids.
Name of the child

This metabolic disorder is called: .....

Fatty acids are found in fatty foods, and are used for energy production in the body’s cells.

In case of a ..... , long-chain fatty acids cannot be used for energy
Name of the metabolic disorder

production. In case of an insufficient or incorrect diet, an energy deficiency can occur which results in e.g. low blood sugar (hypoglycaemia) or muscle pain.

What can the child eat and can he or she not eat?

..... must have ☐ a low-fat ☐ strictly low-fat diet.
Name of the child

The parents or the managing metabolic team will provide you with a detailed overview.

..... has an emergency health card ☐ yes ☐ no
Name of the child

If yes, obtain a copy from the parents

What do meals together look like?

Allowed foods: Fruit, vegetables, cereals, bread without butter / nuts / kernels, potatoes, rice, pasta without egg, milk / yoghurt with 0.1 - 1.5 % fat, low-fat cheese (consult the parents), low-fat curd cheese, light cream cheese, boiled ham and rolled fillet of ham, corned beef, chicken breast cold cuts, poultry without skin, lean pork or beef, coalfish, rose fish, cod, water, tea, lemonade, juice, marmalade, honey, fruit gums, grape sugar, lollipops, ice lollies, alphabet biscuits, salt sticks, ketchup, MCT fats (see below)

Prohibited foods: Croissant, bread with nuts / kernels, sweet yeast butter bread, whole milk, yoghurt 3.5 % fat, cream, sausage spread, salami, cold cuts, bockwurst (veal and pork sausage), bratwurst (grill sausage), fatty fish, salmon, egg, standard oil, butter, margarine, hazelnut spread, mayonnaise, chips, fried potatoes, casserole, cream soups, cream sauces, cakes, biscuits, dairy ice cream, crackers, chocolate

What do meals together look like?

Always discuss with the child what he or she can eat in a meal. For instance, the range can be supplemented with a piece of low-fat meat, or the child can bring food from home. Facilities with their own kitchen can adapt recipes, e.g. cook rice pudding with semi-skimmed milk.
The child **must** eat something at mealtimes. The calculated amount of food and energy is determined by the metabolic team. Fasting phases of more than ..... hours should be avoided.

How can food preparation be made easier?

- Discuss menu options or “special meals” with the food supplier / or cook, if in house catering
- Have suitable foods in stock to supplement or replace meals
- Small dishes or supplements can potentially be prepared in the facility, e.g. potatoes
- Parents should be informed in advance by the facility about birthdays, trips, cooking events

What is MCT fat?

“Normal fat” is largely replaced by MCT fat, which consists of medium-chain fatty acids. There is MCT margarine, MCT oil and MCT fat powder. The parents will inform you on the precise quantities. It is important that the child also eats this fat! MCT fat is food, not medicine. If, once in a while, the child doesn’t want to eat MCT fat, he or she won’t be at risk of any serious danger, but the parents must be informed about it.

What emergency situation can occur if the child eats something that he or she shouldn't eat?

A therapy mistake doesn’t necessarily put the child in **any serious danger**! Despite this, a continuous therapy is crucial for the long-term course and the health of the child.

What must be done in case of vomiting, fever, refusal of food?

The parents must be informed promptly so that they can decide how to proceed.
If required, the child must be picked up e.g. in case of vomiting / fever.

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