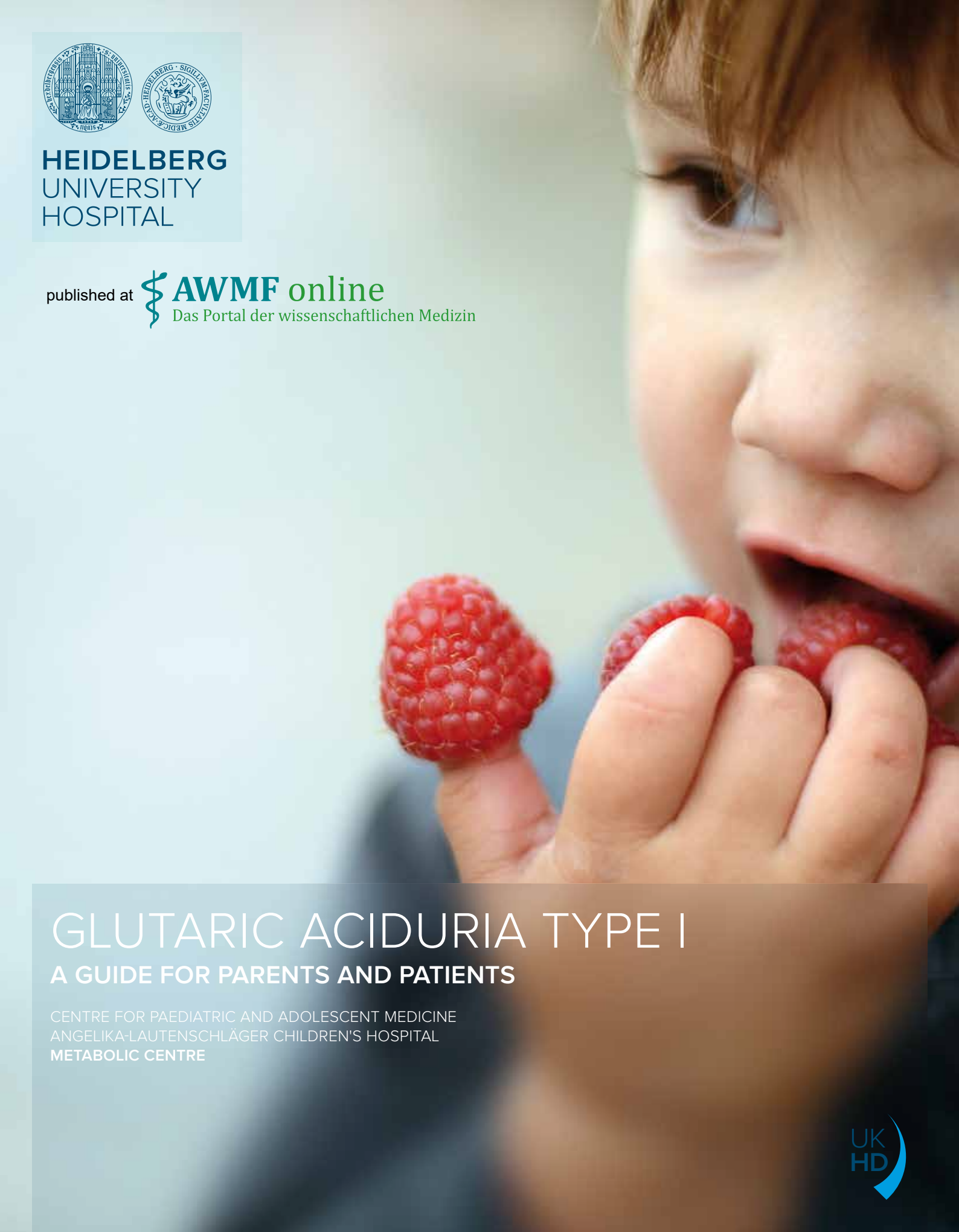

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GLUTARIC ACIDURIA TYPE I

A GUIDE FOR PARENTS AND PATIENTS

CENTRE FOR PAEDIATRIC AND ADOLESCENT MEDICINE
ANGELIKA-LAUTENSCHLÄGER CHILDREN'S HOSPITAL
METABOLIC CENTRE

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CONTENTS

PREFACE AND OBJECTIVE OF THE GUIDE

Your child (or you) has been diagnosed with glutaric aciduria type I. This diagnosis has certainly raised a number of questions and may also have given rise to some concerns. You have probably neither heard of this inherited metabolic disorder before, nor do you know anyone else who has been diagnosed with this disease. Moreover, you may find it difficult to "understand" this disease, especially if your child (or you) does not show any apparent signs or symptoms.

This 2nd updated edition of this guide is therefore directed primarily at parents and patients. It is designed to answer the most frequent questions, give you a general idea of what glutaric aciduria type I is and how this disease is treated according to the present state of knowledge. Secondly, this guide is addressed to all professional groups that provide treatment to children, adolescents and adults with glutaric aciduria type I.

We hope that this guide will provide you with additional, hands-on support during the daily treatment. However, this guide is in no way intended to replace a structured initial consultation or the medical care and continuous training provided by the experienced team of a metabolic centre. Any change in the treatment should always be made in consultation with the attending team of metabolic experts.

CURRENT GUIDELINE FOR GLUTARIC ACIDURIA TYPE I

All recommendations given in this guide conform to the current guideline (AWMF Guideline No. 027/018, highest quality class "S3", i.e. evidence- and consensus-based guideline) for the "Diagnosis, Therapy and Management of Glutaric Aciduria Type I (synonym: glutaryl-CoA dehydrogenase deficiency)". The guideline was developed by an international guideline development group and published for the first time in 2007. Besides Germany, the guideline also became a national therapy guideline in other countries (including Italy, Portugal and the Netherlands).

The first revision of the guideline (2011) was based mainly on the results of a study on 52 patients who were identified by newborn screening in Germany. This study was the first to demonstrate the positive effect of guideline-based treatment on the clinical outcome (Heringer et al. 2010). This was taken as a basis for developing the 1st edition of this guide for parents. Over the last few years, collaboration on a national and international scale has made it possible to further expand the knowledge on the disease and further increase the evidence level of the guideline recommendations.

In 2016, the guideline was revised for the second time, which forms the basis for this 2nd updated edition of the guide for parents. The current guideline still has the highest AWMF quality class "S3". It consolidates the more than thirty years of experience of international experts and meets the high requirements for objectivity, transparency, evidence base and consensus development. In addition, the guideline takes into account additional criteria that are important for the treatment process, such as clinical relevance and experience, consistency of evidence, benefits and risks for the patient, the perspective of the patient and the families, ethical, legal and economic aspects, the applicability to the German health care system as well as practicability in daily life. According to the present state of knowledge, the current guideline recommendations are the most effective to best protect your child's (or your) health and development. The complete guideline can be obtained via the online portal of the Association of the Scientific Medical Societies in Germany (AWMF) (www.awmf.org/; main menu: "Guidelines"). It predominantly addresses all professional groups that provide treatment to patients with glutaric aciduria type I.

Even though the guideline and this guide have been prepared with the utmost care, they may contain inconsistencies or even mistakes. In addition, not all patients may benefit from the recommended treatment to the same extent. Therefore, no guarantee can be given as to the use of this guide and the therapeutic outcome. The practical implementation of the recommended treatment and the associated duty of care are solely incumbent upon the attending physician.

Kind regards,

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P.S.: We will be happy to receive any suggestions for continuously improving the brochure.

DIAGNOSIS

If there is a confirmed diagnosis of glutaric aciduria type I, other family members (in particular siblings and parents) of the affected patient should be specifically tested for the disease as well.

WHAT DOES “GLUTARIC ACIDURIA TYPE I” MEAN?

The term “glutaric aciduria” means “presence of glutaric acid in the urine”. Glutaric acid is an intermediate breakdown product of human metabolism. It is usually present in the body in small quantities only and is excreted in the urine. Increased excretion of glutaric acid had already been observed in patients with glutaric aciduria before the actual cause of the disease was discovered more than 40 years ago. This first-observed biochemical symptom gave the disease its name. Since there are other diseases involving increased excretion of glutaric acid, these diseases were classified into three types (type I, type II and type III). This guide exclusively addresses glutaric aciduria type I. Even though the names glutaric aciduria type II and type III sound very similar, they are different diseases, which must not be confused with glutaric aciduria type I.

HOW IS THE DISEASE DIAGNOSED?

Besides increased excretion of glutaric acid, glutaric aciduria type I involves the presence of other substances in the urine and other body fluids, such as 3-hydroxyglutaric acid and glutarylcarnitine. In people who are not affected by the disease, these substances are present in the body and blood in very small quantities only and are excreted in the urine. These small quantities are also referred to as the “normal range” or “reference range”. In affected patients, by contrast, these substances are present in increased concentrations, which are often many times above the normal range. As a result, most affected children can already be reliably identified by newborn screening. According to the German national guidelines for newborn screening (www.g-ba.de: Guidelines for children: Expanded newborn screening), all newborns throughout Germany have been tested for glutaric aciduria type I as part of the early detection screening since 1 April 2005. On average, about 6–7 newborns are diagnosed with glutaric aciduria type I in Germany every year, which is equivalent to a prevalence of one newborn with glutaric aciduria type I in 120,000 newborns (1:120,000).

To ultimately confirm the diagnosis, additional testing is necessary (molecular-genetic and, if necessary, enzymatic testing).

CAN OTHER FAMILY MEMBERS ALSO BE AFFECTED BY THE DISEASE?

Yes, this is possible. Since the disease is inherited, other close family members may be affected as well. This may even be the case if no apparent symptoms are present in them.

NATURAL DISEASE COURSE

HOW DOES THE DISEASE MANIFEST?

Newborns and young infants
Most newborns and young infants with glutaric aciduria type I do not develop any symptoms and cannot be distinguished from healthy children of the same age. Some newborns and young infants are affected by mild, usually temporary neurological disorders, such as reduced muscle tone (truncal muscular hypotonia) and asymmetric movement patterns which may lead to mild delays in motor development. However, such symptoms are generally quite common in infants and improve spontaneously or through physical therapy. Another symptom that affects most children with this disease is a large head circumference (macrocephaly). However, since 3% of all people have an enlarged head and glutaric aciduria type I is a very rare condition, there are much more people with a large head without glutaric aciduria type I than people affected by this disease. Therefore, it is almost impossible to identify affected newborns and young infants without newborn screening.

Older infants and toddlers
If the disease remains undiagnosed and untreated, permanent damage to a particular area of the brain (basal ganglia) occurs mostly in older infants and toddlers, which may result in an irreversible movement disorder. The most common movement disorder in glutaric aciduria type I is called dystonia. It is characterised by limited or absent interaction between various muscle groups, which are very important for all movements. As a consequence, affected children may lose many of their previously acquired motor abilities and are then highly dependent on help from their environment. Many children additionally develop speech and swallowing problems affecting normal food intake and increasing the risk of aspiration. In contrast to these pronounced physical changes, the cognitive abilities of many affected children remain intact. Some patients have completed their school education, vocational training and university studies despite their existing handicaps.

The above-described changes in the brain typically develop during or shortly after a febrile infectious disease (gastrointestinal infection, pneumonia), especially if accompanied by strongly reduced nutrient and fluid intake or extensive nutrient and fluid loss due to vomiting and diarrhoea. Other triggers, for example surgeries and vaccinations, have been reported as well. This so-called acute encephalopathic crisis may occur up to the age of 6 years. As far as is known today, such crises do not occur in older children. The ultimate goal of the treatment starting already at neonatal age is to prevent an acute encephalopathic crisis and its consequences.

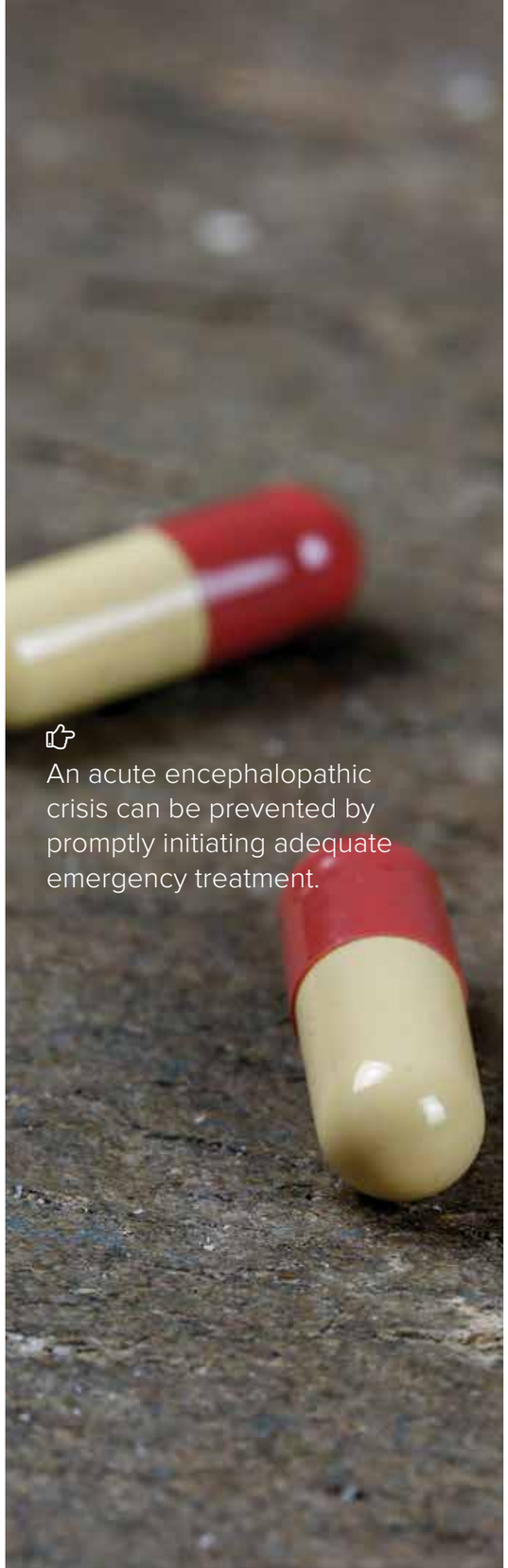
Adolescents and adults
By now, individual adolescents and adults with glutaric aciduria type I have been identified who have come through childhood unscathed, despite not having been diagnosed and treated (“late-onset type”). The physical symptoms in adolescence and adulthood differ from those in childhood. The disease manifests itself primarily by ataxic gait, reduced fine motor skills and tremor, headaches, and vertigo. At a more advanced age, signs of dementia may occur. Unlike in childhood, the detectable changes in the brain do not affect the basal ganglia, but predominantly what is referred to as the white matter. The white matter consists of nerve fibres and their sheaths (myelin). The changes in these patients are believed to occur due to the many years of exposure to the metabolic products accumulating in the brain.

In addition, some adolescent and adult patients may develop renal dysfunction.

Furthermore, some asymptomatic mothers affected by the disease have been identified during the newborn screening (initially showing abnormal results, which normalised later on) of their children (maternal GA-I).

HOW DO I RECOGNISE AN ACUTE ENCEPHALOPATHIC CRISIS?

According to the present state of knowledge, it is not possible to accurately determine the exact onset of an acute encephalopathic crisis. The symptoms begin insidiously and then tend to progress rapidly, leading to mostly irreversible changes. The emergence of the first symptoms often coincides with an infectious disease involving fever, fatigue, lack of appetite and reduced food intake. Gastrointestinal infections additionally involve vomiting and diarrhoea, which should always be seen as warning signals, even if no fever is present. In the second phase, which can often last for one to three days, the initial symptoms get worse and the level of alertness may become gradually impaired, which is why affected children can often not be woken up and do not or hardly respond to strong external stimuli (coma/precoma). Eventually, a change in muscle tone often occurs all of a sudden (“out of nowhere”, “like a stroke”). Affected children initially show very weak muscle tone (muscular hypotonia), which then develops into dystonia within a few days.



OTHER DISEASE FORMS

In addition, there are individual patients who develop insidious neurological symptoms without experiencing an acute crisis event (insidious-onset type). These patients are usually affected by a milder form of dystonia than patients who have suffered from an encephalopathic crisis. The insidious-onset type is particularly observed in patients who did not receive adequate dietary treatment according to the guideline recommendations.

WILL THE DISEASE DISAPPEAR OVER THE COURSE OF LIFE?

No. Glutaric aciduria type I is an inherited disease, so it does not disappear spontaneously over the course of life. It is known that in the course of the disease permanent, often severe damage to the brain may occur during the first 6 years of life. If damage to the brain during this period is prevented through early diagnosis and treatment according to the guideline recommendations, children have good chances of continuing to develop normally. If damage occurs during this period, the changes will be permanent and can only be mitigated by treatment. The long-term course of the disease in adolescence and adulthood is still unknown and is therefore the subject of current studies.

PATHOGENESIS

HOW DOES THE DISEASE DEVELOP?

Glutaric aciduria type 1 is an inherited metabolic disorder. Metabolic disorders are caused by an inborn defect in the synthesis, conversion or degradation of body substances or food components. The body requires a multitude of enzymes for these reactions. Enzymes act as catalysts, meaning they accelerate the above-mentioned processes in our body. If a specific enzyme does not function properly, changes will occur in metabolic processes. Some of these changes cause diseases – as is the case with glutaric aciduria type I.

In glutaric aciduria type I, a specific enzyme is not functioning. It is called glutaryl-CoA dehydrogenase and is involved in the breakdown of specific protein components (amino acids). A defect in glutaryl-CoA dehydrogenase affects the breakdown of the amino acids lysine, tryptophan, and hydroxylysine, resulting in an accumulation of specific metabolic products, which can be detected in the urine and blood (Fig. 1). If the enzyme's function is lost completely, the excretion of these metabolic products in the urine is strongly increased (high excreters); if there is residual function, the excretion of these substances is only slightly increased or may even be normal (low excreters). The function of the affected enzyme cannot be performed by any other enzyme.

WHY DOES THE DISEASE AFFECT THE BRAIN?

Studies in cell cultures and animal models have shown that high concentrations of some metabolic products accumulating in glutaric aciduria type I can have a harmful effect on the brain (neurotoxicity). In addition, the metabolic products in glutaric aciduria type I have been shown to accumulate particularly strongly in the brain, from where they are more difficult to remove. The amount of metabolic products in the brain is increased by a high-protein diet or a lack of energy, and is lowered by reduced protein or lysine intake and sufficient energy supply.

Moreover, additional factors are assumed to play a role in the development of an acute encephalopathic crisis. These include an insufficient supply of energy and indispensable (essential) nutrients to the body in febrile infectious diseases (catabolism). In such situations, the body mobilises its own resources, releasing muscle protein and thereby also lysine.

WHY IS MY CHILD AFFECTED EVEN THOUGH I AM HEALTHY?

Parents and their families are often very confused when a child is affected by a specific disease even though both parents and other family members are healthy. This frequently leads to doubts about the correctness of the diagnosis, or the affected paternal (or maternal) family denying “responsibility” for this genetic disorder and attributing it to the maternal (or paternal) family (“We've never had anything like that in our family” “That must be from you”). This often causes an additional burden and uncertainty, especially for mothers of newly diagnosed children.

However, it is actually not contradictory for a genetic disorder to occur in a family that has no history of genetic disorders; on the contrary, it is typical of a specific inheritance pattern called autosomal recessive inheritance. This means the father and the mother each pass on to their child one piece of defective genetic information (gene), in this case, for the enzyme glutaryl-CoA dehydrogenase. The parents themselves each still have one intact gene for this enzyme and are therefore not affected. They are carriers of this disease without being affected themselves.

Every individual has two sets of genes – one from the mother and one from the father. The genes are the equivalent of a page in a cookbook, meaning they contain the recipe for a specific “dish”. In autosomal recessive diseases, one intact gene is enough to prevent a disease from occurring. Only when two incomplete genes are combined does the disease manifest itself. Every child only inherits half of the maternal and paternal genetic information to prevent the genetic material from being doubled in the next generation. That is why carriers of a specific disease may have healthy or affected children. Two-thirds of healthy children are carriers themselves (Fig. 2).

In an affected family with four children, there are on average three healthy children (two of whom are carriers) and one child who has the condition. However, this is only a mathematical assumption and does not apply to many families in real life. That is why there are many families who have only healthy or only affected children. But the presence of one healthy or affected child in a family has no influence on whether the next child in that family will be healthy or affected. It is similar to rolling a die, where every roll can result in a number between one and six: All children in the family have the same probability of being healthy or affected.

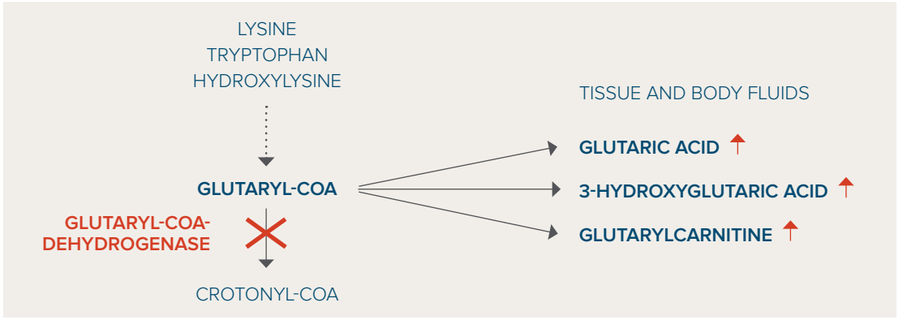


FIGURE 1 (top)
CAUSE OF GLUTARIC ACIDURIA TYPE I
Glutaryl-CoA dehydrogenase catalyses an individual step in the final common catabolic pathways of the amino acids lysine, hydroxylysine, and tryptophan. In terms of quantity, the breakdown of lysine is more significant than that of tryptophan and hydroxylysine. The congenital enzyme defect in glutaric aciduria type I causes an accumulation of specific metabolic products (glutaric acid, 3-hydroxyglutaric acid, glutarylcarnitine).

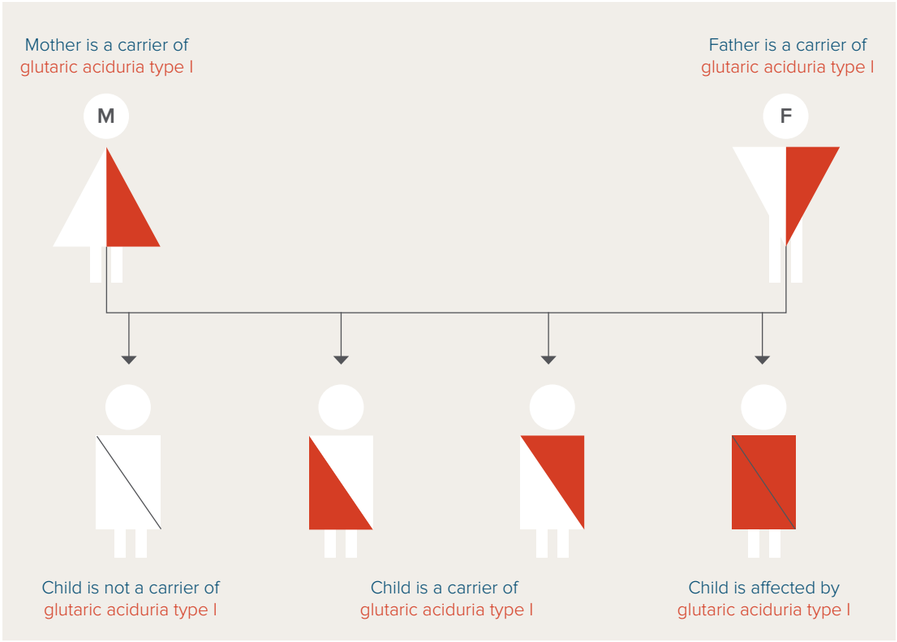


FIGURE 2
AUTOSOMAL RECESSIVE INHERITANCE IN GLUTARIC ACIDURIA TYPE I
Dark red triangles symbolise defective/incomplete genes, white triangles symbolise intact, complete genes.

To better understand these complex relationships and to consider them in family planning, in-depth genetic counselling at an institute for human genetics is strongly recommended.

DID I DO SOMETHING WRONG DURING PREGNANCY?

No. Although the occurrence of specific diseases, the use of certain medications, alcohol and other drugs as well as health behaviour during pregnancy have a major influence on the health of a newborn, there is no reasonable cause to believe that glutaric aciduria type I is the result of having done “something wrong” during pregnancy. No such connections are known. The above-described genetic changes are much more likely to have been passed from parents to their children within one family over many generations. Since carriers of glutaric aciduria are not affected by the condition, this inheritance of defective genes went unnoticed. Every individual carries several genetic changes that can be passed on to their children without being noticed. Genetic changes can generally occur spontaneously in anyone.

DIET AND CARNITINE

CAN GLUTARIC ACIDURIA TYPE I BE TREATED?

The natural course of glutaric aciduria type I can be positively influenced by treatment if 1) the diagnosis is made before the first permanent neurological symptoms occur (newborn screening and confirmational diagnostic work-up) and 2) treatment is initiated at an early stage to prevent permanent, severe damage to the brain. The currently recommended therapy comprises a metabolic maintenance treatment – consisting of a low-lysine diet and carnitine supplementation – as well as temporary intensified emergency treatment during febrile infectious diseases, fasting periods before and after surgeries and in the event of febrile reactions to vaccinations. It is currently assumed that these measures can prevent an acute encephalopathic crisis in about 90% of all children diagnosed at an early stage. By contrast, an asymptomatic disease course without treatment is only expected in a small minority of patients (about 5–10%). This clearly attests to the benefits of the currently recommended treatment.

The therapeutic outcome depends largely on providing parents and patients with sufficient information and training. Parents and their children should receive comprehensive information and training as well as appropriate written materials from an interdisciplinary team of metabolic experts. Training sessions should be repeated and supplemented at regular intervals.

WHO SUPERVISES THE TREATMENT?

The prescription of any dietary treatment and medication requires a risk/benefit assessment by experts experienced in this treatment. In order to manage problems associated with this disease or the recommended therapy and to successfully perform the treatment, the treatment should be initiated and controlled by an interdisciplinary team of paediatric experts in metabolic medicine, paediatric dieticians, nursing staff, physical therapists, speech therapists, occupational therapists (in the event of eating disorders) as well as psychologists. Regular follow-ups at a metabolic centre increase the probability of an asymptomatic course.

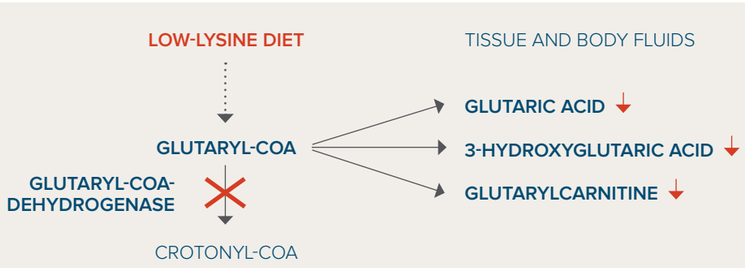


FIGURE 3
LOW-LYSINE DIETARY TREATMENT
In terms of quantity, lysine is the most important amino acid precursor of the metabolic products that accumulate in glutaric aciduria type I (glutaric acid, 3-hydroxyglutaric acid, glutarylcarnitine). Limiting the lysine intake in the diet reduces the accumulation of these metabolic products in the body, especially in the brain.

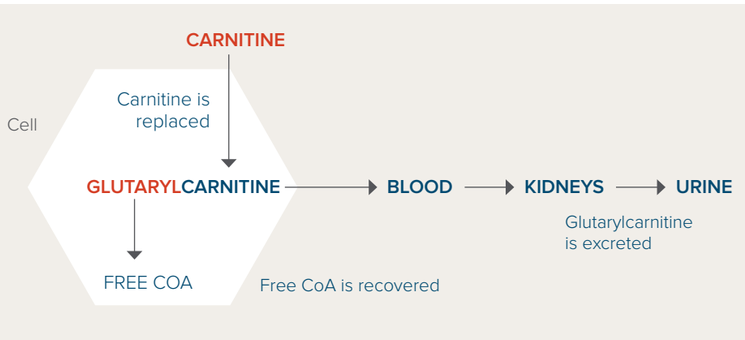


FIGURE 4
TREATMENT WITH CARNITINE
The accumulating glutaryl-CoA attaches to the transport substance carnitine, enabling it to leave the cells in the form of glutarylcarnitine and ultimately be excreted in the urine. This releases free CoA in the cell, making it available for other metabolic reactions. However, the body loses a lot of carnitine during this detoxifying reaction. This loss is replenished with the carnitine juice.

HOW DOES THE LOW-LYSINE DIET WORK?

Limiting the intake of the amino acid lysine, which cannot be properly broken down in glutaric aciduria type I, considerably reduces the development of harmful metabolic products in the body, thereby reducing their accumulation in the brain (see Fig. 3). However, the treatment is not expected to fully normalise the level of these metabolic products.

A low-lysine diet should be used in all children who have not suffered from an acute encephalopathic crisis by the time the diagnosis is made. This includes all newly diagnosed newborns. The benefit of dietary treatment is unclear in children who were only diagnosed after having suffered an acute encephalopathic crisis. One possible effect is to prevent further crises or to stop a progressive deterioration of the neurological problems.

Dietary treatment in glutaric aciduria type I should be based on the general, age-dependent and individual daily nutritional requirements. This is absolutely essential to enable normal growth and development. The diet follows the dietary recommendations of national and international expert societies (e.g. D-A-CH, WHO) outlining the age-dependent minimum requirements of a growing child.

The practical application of dietary treatment is explained in greater detail in the second part of the guide. In addition, the appendix provides you with current food composition and nutrition tables and further useful materials on dietary treatment.

CARNITINE

Carnitine is an important transport substance in the human body that is mainly taken in through food. Carnitine attaches to glutaryl-CoA (see Fig. 1 and 3) that forms in the body's cells and produces glutarylcarnitine. Glutarylcarnitine is released into the bloodstream and then excreted in the urine via the kidneys. This is a physiological detoxifying strategy of the body to reduce the accumulation of harmful metabolic products and increase the available amount of free coenzyme A (CoA), an important substance in many metabolic reactions (see. Fig. 4). However, the body loses so much carnitine during this important reaction that it cannot be sufficiently replenished from food, resulting in carnitine deficiency. Carnitine deficiency is harmful for the body, because carnitine also performs other functions. Most notably, it attaches to long-chain fatty acids, enabling the body to access its own fat reserves as an important source of energy.

Administering carnitine therefore serves several purposes: 1) Supporting the body in detoxifying itself from accumulating metabolic products, 2) Increasing the availability of free CoA and 3) Preventing secondary carnitine deficiency. Lifelong carnitine supplementation is an important pillar of treatment and has a positive effect on the disease course. This has also been confirmed in patients who have already suffered from an acute encephalopathic crisis. The carnitine dose is adjusted by the attending team of metabolic experts based on age, weight, and the concentration of free carnitine detectable in the blood. The recommended starting dose is 100 mg carnitine per kg body weight (divided into 3 single doses). In some children, the use of carnitine may cause strong (fishy) body odour and diarrhoea. In that case, reducing the dose can be attempted after consulting the attending team of metabolic experts.

Reducing or even discontinuing the daily administration of carnitine without consulting the attending team of metabolic experts is strongly advised against!!

RIBOFLAVIN (VITAMIN B2)

The enzyme glutaryl-CoA dehydrogenase, which is affected in glutaric aciduria type I, requires riboflavin (vitamin B2) as a co-factor to function properly. That is why a daily dose of riboflavin has been administered in hopes of increasing the reduced activity of the defective enzyme. However, no recent study has been able to prove that riboflavin actually has a positive influence on the course of the disease. This can likely be explained by the fact that the defective enzyme can only very rarely be stimulated by riboflavin to a relevant extent. There is currently no reliable method available to test riboflavin sensitivity or predict it based on molecular-genetic studies.

Riboflavin often causes stomach aches, nausea and vomiting.

EMERGENCY TREATMENT

WHAT SITUATIONS ARE DANGEROUS FOR MY CHILD?

Combined metabolic maintenance treatment (low-lysine diet, carnitine supplementation) alone is not sufficient for children with glutaric aciduria in the first 6 years of life to be protected against an acute encephalopathic crisis in some situations. Intensified emergency treatment is required if a potentially dangerous situations occurs. This includes febrile infectious diseases (especially when accompanied by vomiting and diarrhoea), febrile reactions to vaccinations and surgeries as well perioperative fasting periods. Since there is a stealthy transition between the first signs of a febrile infectious disease and permanent damage to the brain, the exact onset of a crisis cannot be determined with certainty. That is why swift emergency treatment as well as gradual intensification is strongly recommended in any (!) potentially dangerous situation.

HOW DOES THE EMERGENCY TREATMENT WORK?

Intensified emergency treatment has the same aims as combined metabolic maintenance treatment, but uses more powerful methods. The most important principles of emergency treatment are as follows:

— High energy supply (additional administration of insulin, if necessary): This can prevent or eliminate a lack of energy or nutrients (catabolism), which is important to reduce the development of harmful metabolic products. In febrile infectious diseases and during perioperative fasting periods, the body has increased energy requirements (rule of thumb: a rise in body temperature by 1°C increases the body's energy requirements by about 10%).

— Reducing or temporarily interrupting protein supply: If the body is lacking energy, the protein in the body (muscle tissue) and that in food is used for energy generation, resulting in an increased amount of harmful metabolic products. The supply of natural protein is therefore temporarily reduced or stopped completely. Lysine-free amino acid supplements can continue to be administered if they are tolerated by the affected child. The high energy supply and release of insulin strongly stimulates protein synthesis in the body's cells. That is why the normal amount of protein is tolerated again after a relatively short period of time. The protein supply should therefore not be interrupted for longer than 24 hours.

— Increasing the carnitine supply: By doubling the carnitine dose or administering carnitine intravenously, the body's physiological detoxifying function (production of glutarylcarnitine) is supported and carnitine deficiency is effectively prevented.

— Restoring the fluid, electrolyte and acid/base balance: Febrile infectious diseases often involve an increased loss of fluids, electrolytes and bases (sweating, diarrhoea, vomiting), while their intake is reduced at the same time. Swiftly normalising any sustained deficits and adequately replenishing any remaining losses is necessary to promote the healing processes. In addition, an adequate intake of fluids and bases promotes the excretion of harmful metabolic products in the urine.

— Energy-“saving” measures: Fever-reducing measures (physical and medication-based) should be used liberally, because an elevated body temperature leads to increased energy requirements. Temporary treatment of an increased vomiting tendency is helpful to reduce nutrient and fluid losses due to repeated vomiting and in order to be able to return to a normal diet.

CAN I START/PERFORM EMERGENCY TREATMENT AT HOME?

Emergency treatment is designed as a stepwise regimen, meaning there is a regimen for treatment at home and one for the hospital. However, emergency treatment at home is only recommended if the child's condition allows it, the child's parents have received appropriate training, and the attending team of metabolic experts is regularly informed about the child's condition. Based on our experience, emergency treatment at home is not recommended for newborns and infants, and should instead be done at the attending hospital. From the medical point of view, the following conditions should be met to perform emergency treatment at home:

— The body temperature is below 38.5°C.
— The child is not vomiting and is eating normally.
— There are no alarming symptoms, such as vomiting, diarrhoea, extreme fatigue, muscle weakness, movement disorders.

TARGET ASPECT	PROPOSED STRATEGY
EDUCATION AND TRAINING OF PARENTS	Parents are informed in detail about the course of the disease and particular risks. They are given specific instructions on how to perform the treatment. Training sessions are held at regular intervals by the supervising metabolic centre. The continuous training sessions are also designed to raise awareness of the disease.
TREATMENT PROTOCOLS/ EMERGENCY CARD	Written treatment protocols are handed out to all involved (parents, metabolic centres, local hospitals, paediatricians) and are regularly updated and adapted to any changes. In addition, parents are given an emergency card containing a brief overview of the key information and the phone number of the supervising metabolic centre.
SUPPLIES	Parents should be advised to maintain sufficient supplies of the required special dietetic products and medications (this also applies when going on holiday, etc., see below).
CLOSE COOPERATION WITH LOCAL PAEDIATRIC HOSPITALS AND PAEDIATRICIANS	The local paediatric hospital or the paediatrician is contacted and informed by the supervising metabolic centre. Any relevant documents and information (incl. written treatment protocols) are handed over by the metabolic centre in written form in a timely manner. Inpatient emergency treatment can be started at the local paediatric hospital if the supervising metabolic centre is far away. The metabolic centre is informed immediately after the patient has been admitted and coordinates the further course of emergency treatment.
HOLIDAY MANAGEMENT	Metabolic specialists/centres at the holiday destination are informed in writing about the disease and the current treatment protocols with the parent's approval before going on holiday. The parents receive the contact address, phone number and email address of the supervising colleague/metabolic centre.
CONSULTATION IN THE EVENT OF INFECTIOUS DISEASES	Parents are instructed to contact the supervising metabolic centre if the body temperature rises above 38.5 °C and clinical signs of an infectious disease or neurological symptoms occur. The emergency treatment and, if necessary, inpatient admission to the local paediatric hospital is coordinated by the metabolic centre.
SURGERY MANAGEMENT	In the event of elective surgeries, the supervising metabolic centre is informed in advance by the surgeons and anaesthesiologists to determine the perioperative metabolic management. Whenever possible, pre- and post-operative monitoring should be done at a metabolic centre. In the event of emergency surgeries, the metabolic centre is informed immediately to support the perioperative metabolic management.

TABLE 1 **STRATEGIES TO OPTIMISE EMERGENCY TREATMENT**

Emergency treatment is performed at home for an initial period of 12–24 hours. The child's condition (consciousness, fever, food intake, vomiting, diarrhoea, other signs of illness) is checked every 2 hours. If there is any deterioration, the child should be immediately admitted to the attending hospital for inpatient emergency treatment. If necessary, adequately trained parents can also administer maltodextrin solution via a feeding tube to ensure optimum energy supply (incl. at night). If emergency treatment at home was successful and no alarming symptoms occurred within the first 12–24 hours, the supply of natural protein should be gradually increased over 24–48 hours until reaching the level of the normal dietary plan. This is necessary to prevent protein deficiency, which, in turn, can contribute to a metabolic crisis.

Please see page 35 for recommendations on performing emergency treatment at home. Recommendations on performing emergency treatment at the hospital are not relevant for this guide, since the appropriate emergency treatment protocols are recorded in the child's file at the supervising metabolic centre. In addition, these recommendations can be read in the guideline (www.awmf.org).

HOW CAN I AVOID DELAYS IN EMERGENCY TREATMENT?

Delayed or inadequate emergency treatment during a dangerous situation (febrile infectious disease, febrile reactions to vaccination, surgery) is the most common cause which leads to an acute encephalopathic crisis resulting in permanent neurological problems despite timely diagnosis and treatment.

The problem of delaying or failing to perform emergency treatment is often due to a lack of awareness among parents. However, it may also result from involving “unfamiliar” doctors (accident & emergency department at an unfamiliar hospital, e.g. at a holiday destination, or if the previously attending metabolic specialist is not available or is not notified) who have no experience with the treatment of the child and glutaric aciduria type I. Several optimisation strategies have proved useful to recognise the necessity of emergency treatment and to initiate treatment without delay. These are listed in Table 1 on page 15.

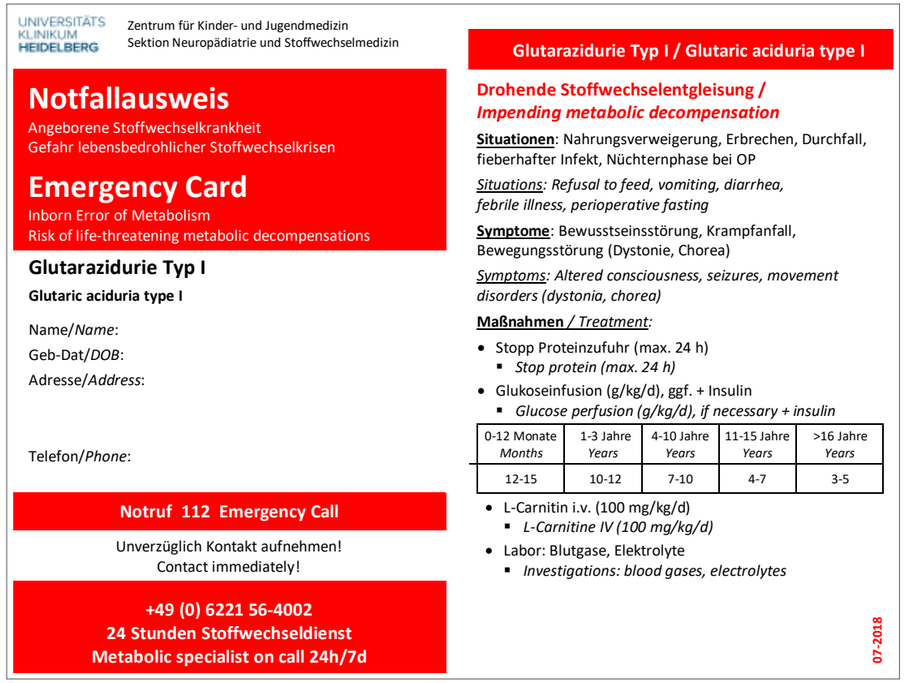
Delayed or inadequate emergency treatment during a dangerous situation (febrile infectious disease, reaction to vaccination, surgery) is the most common cause which leads to an acute encephalopathic crisis resulting in permanent neurological problems despite having been diagnosed and treated as a newborn.

IS EMERGENCY TREATMENT NECESSARY AFTER THE AGE OF 6 YEARS?

Although no acute encephalopathic crisis in a child with glutaric aciduria type I after the age of 6 years has been reported anywhere in the world, it cannot be ruled out with certainty that febrile infectious diseases, reactions to vaccinations and surgeries after the age of 6 years may cause subclinical (i.e. not immediately apparent or only after repeated episodes) neurological damage. Future studies are essential to assess the brain's sensitivity to situations that have been considered to be dangerous up to the age of 6 years (infectious diseases, febrile reactions to vaccinations, surgeries). The guideline development group therefore recommends that emergency treatment in children after the age of 6 years should be considered in the event of severe illness or as part of perioperative management (e.g. when performing a Caesarean section). Emergency treatment is then based on the treatment for the younger age group up to and including 6 years of age.

EMERGENCY CARD

An emergency card, preferably laminated and conveniently sized (e.g. like a credit card), should be issued to every child with glutaric aciduria type I and be carried by the parents or the patient. Issuing multiple copies is recommended if several individuals are involved in caring for the child. In motor vehicles, an emergency card should be placed at a prominent position. Prior to staying abroad, having the emergency card translated into the respective national language (and/or English) is recommended. The emergency card is designed to give a brief overview of key information about glutaric aciduria type I and should include the phone number of the supervising metabolic centre. The emergency card is meant to ensure that any necessary first-aid can be promptly provided in an emergency situation. Dosage information should be periodically reviewed and, if necessary, adapted by the attending metabolic specialist. As an example, the figure below (Fig. 5) shows the emergency card used by the Heidelberg University Hospital's Centre for Paediatric and Adolescent Medicine.


UNIVERSITÄTS KLINIKUM HEIDELBERG

Zentrum für Kinder- und Jugendmedizin
Sektion Neuropädiatrie und Stoffwechselmedizin

Notfallausweis
Angeborene Stoffwechselkrankheit
Gefahr lebensbedrohlicher Stoffwechselkrisen

Emergency Card
Inborn Error of Metabolism
Risk of life-threatening metabolic decompensations

Glutarazidurie Typ I
Glutaric aciduria type I

Name/*Name*:
Geb-Dat/*DOB*:
Adresse/*Address*:

Telefon/*Phone*:

Notruf 112 Emergency Call

Unverzüglich Kontakt aufnehmen!
Contact immediately!

+49 (0) 6221 56-4002
24 Stunden Stoffwechseldienst
Metabolic specialist on call 24h/7d

Glutarazidurie Typ I / Glutaric aciduria type I

Drohende Stoffwechselentgleisung /
Impending metabolic decompensation

Situationen: Nahrungsverweigerung, Erbrechen, Durchfall, fieberhafter Infekt, Nüchternphase bei OP

Situations: Refusal to feed, vomiting, diarrhea, febrile illness, perioperative fasting

Symptome: Bewusstseinsstörung, Krampfanfall, Bewegungsstörung (Dystonie, Chorea)

Symptoms: Altered consciousness, seizures, movement disorders (dystonia, chorea)

Maßnahmen */ Treatment*:

- Stopp Proteinzufuhr (max. 24 h)
  - *Stop protein (max. 24 h)*
- Glukoseinfusion (g/kg/d), ggf. + Insulin
  - *Glucose perfusion (g/kg/d), if necessary + insulin*

0-12 Monate *Months*	1-3 Jahre *Years*	4-10 Jahre *Years*	11-15 Jahre *Years*	>16 Jahre *Years*
12-15	10-12	7-10	4-7	3-5

- L-Carnitin i.v. (100 mg/kg/d)
  - *L-Carnitine IV (100 mg/kg/d)*
- Labor: Blutgase, Elektrolyte
  - *Investigations: blood gases, electrolytes*

07-2018

FIGURE 5
EMERGENCY CARD FOR GLUTARIC ACIDURIA TYPE 1 (SAMPLE)
The emergency card is issued by the supervising metabolic centre. The correctness of the content is verified by the supervising metabolic specialist. The emergency card shown above is sized like a credit card, folded in the middle and then laminated.

TREATMENT OF MOVEMENT DISORDERS

Movement disorders in glutaric aciduria type I are varied and difficult to treat. The efficacy of medications used cannot be precisely predicted and requires the expertise of specialists (neuropaediatricians). This guide for parents and patients therefore does not contain any dosage information and does not deal with this topic in greater detail. This topic is extensively addressed in the guideline (www.awmf.org).

The most common medications (name of active ingredient) used for the treatment of movement disorders in glutaric aciduria type I include baclofen (may also be administered using a pump), benzodiazepines (e.g. diazepam), trihexyphenidyl, tetrabenazine and botulinum toxin A. In individual cases, treatment with zopiclone has also proved effective. Medications without confirmed efficacy in the treatment of movement disorders include antiepileptics (e.g. vigabatrin, carbamazepine, valproate), amantadine and L-DOPA. In addition, valproate should not be used, because it may theoretically have an adverse effect on energy metabolism and may cause carnitine deficiency.

Regarding neurosurgical treatments or deep brain stimulation, which are used in other patients with dystonic movement disorders, there is very little and partly unfavourable experience in glutaric aciduria type I. The long-term benefit of these neurosurgical procedures cannot yet be estimated at present.

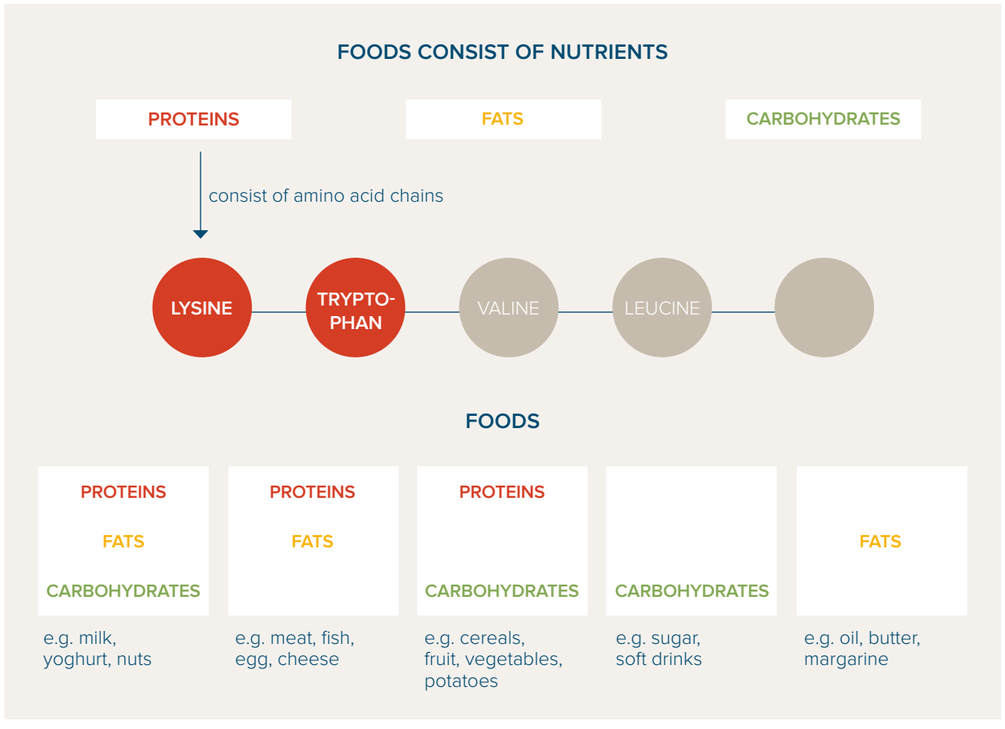
COMPOSITION OF OUR FOOD

Food supplies us with vital nutrients, including the energy-supplying macronutrients protein, fat and carbohydrates as well as the micronutrients vitamins, minerals and trace elements, which do not supply energy.

Glutaric aciduria type I is a disorder that affects the nutrient protein. Food protein serves the body predominantly as building material for organs, muscles, and cells, for example. But the regulatory substances (enzymes, hormones) and protective substances (antibodies) in the body also consist of proteins. All proteins are composed of 20 different building blocks, referred to as amino acids. The amino acids are combined in different orders to form long chains. Eight of these amino acids are essential (vital). This means that they need to be taken in through food in sufficient quantities, because they cannot be synthesised by the body.

The nutrients our foods are composed of are found in the foods in different quantities and concentrations. Foods that contain all three macronutrients include, in particular, milk, yoghurt and nuts. The nutrient combination of protein and fat is contained primarily in meat, fish and cheese. Foods with only one type of nutrient contain either only carbohydrates (e.g. sugar and soft drinks) or only fat (e.g. vegetable oils and margarine).

FIGURE 6
COMPOSITION OF OUR FOOD



FOOD CLASSIFICATION FOR THE LOW-LYSINE DIET

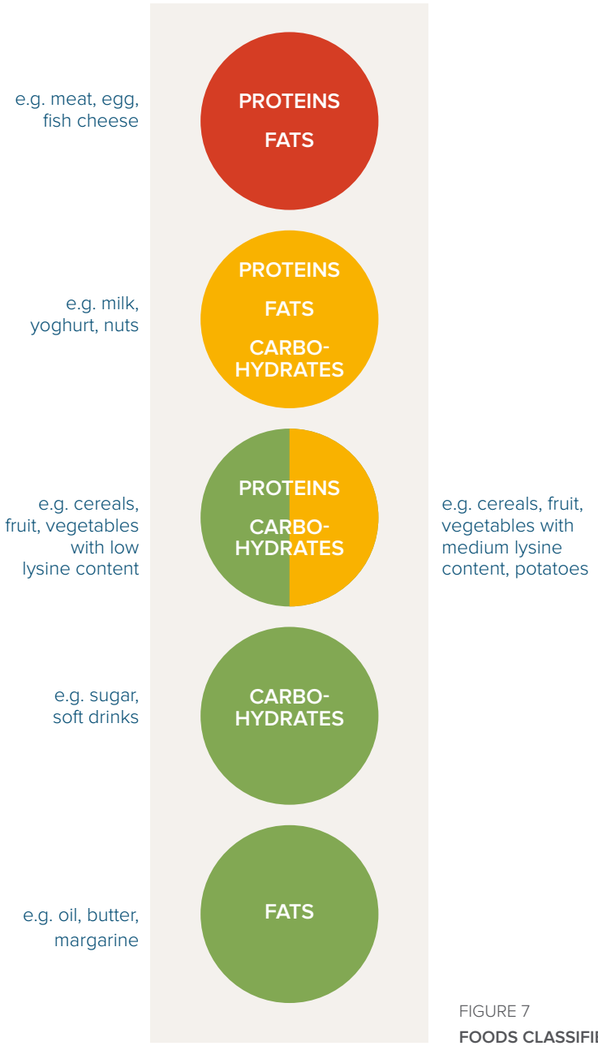


FIGURE 7
FOODS CLASSIFIED BY TRAFFIC LIGHT COLOURS

GREEN GROUP
It comprises low-lysine and lysine-free foods. These foods can be pooled into what is called a daily lysine allowance (see page 32). Weighing and calculating these foods on a daily basis is thus not necessary. Foods of the green group usually make up half to three-quarters of the specified daily lysine intake.

YELLOW GROUP
It comprises foods with a medium lysine content, which are suitable for the low-lysine diet, but can only be consumed in limited amounts. They need to be weighed and calculated. Some of these foods are necessary to reach the specified daily lysine intake.

RED GROUP
Due to their high lysine content, these foods are not suited for patients with glutaric aciduria type I.

COMPOSITION OF THE DIET

DIET IN THE FIRST YEAR OF LIFE

Breastfed infants
The infant is fed a defined amount of lysine (LYS)-free and tryptophan (TRP)-reduced special formula and is additionally breastfed as needed. The amount of breast milk does not need to be measured.

Non-breastfed infants
The infant is fed a defined amount of normal baby formula.

In addition, a lysine (LYS)-free and tryptophan (TRP)-reduced special formula is fed as needed. The infant can drink this formula without limitation.

From the 5th to 6th month of life, complementary food is added to the baby formula, starting by adding the concentrated amino acid supplement.

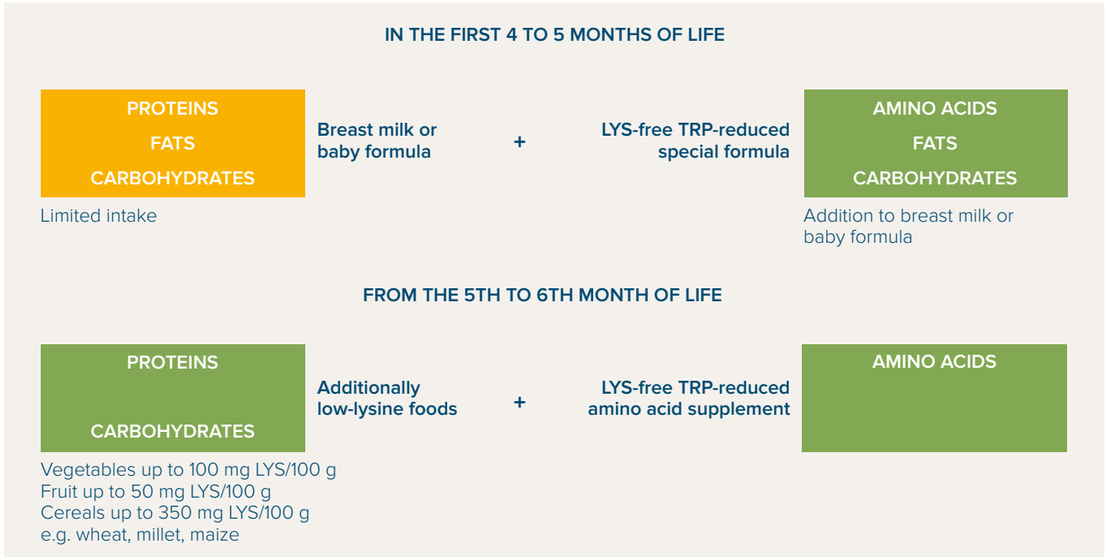


FIGURE 8 **DIET IN THE FIRST YEAR OF LIFE**

DIET AT THE FAMILY TABLE

After the first year of life, the foods of the green group represent the basic foods in the child's diet, supplemented with foods from the yellow group.

The child is allowed to eat many foods from the family's menu, such as:

— Bread/rolls, pasta, rice, potatoes and dumplings
— Vegetables (except for legumes), lettuce, fruit
— Pancakes, waffles, pies and cakes of puff pastry, shortcrust pastry, yeast dough and cake batter. To reduce the lysine content, the cake can be prepared without eggs and/or milk.

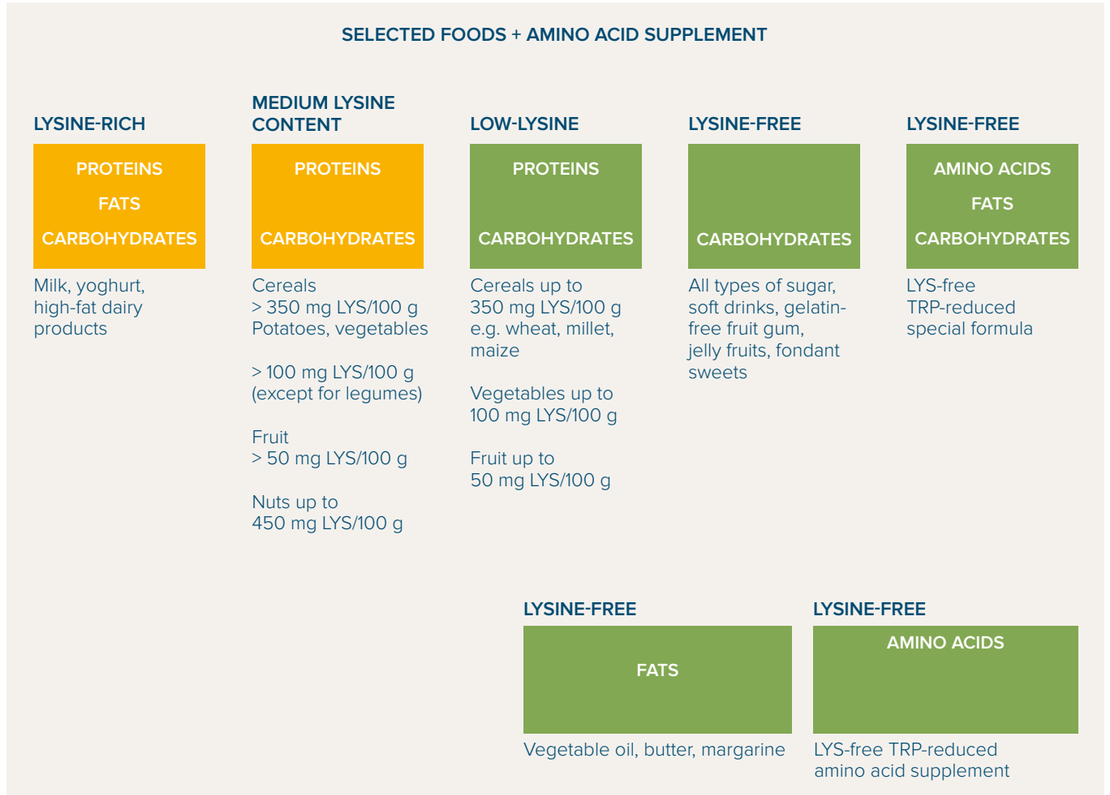


FIGURE 9 **DIET AFTER THE FIRST YEAR OF LIFE**

PRINCIPLE OF DIETARY TREATMENT

LYSINE AND TRYPTOPHAN ARE THE PRECURSORS OF THE HARMFUL SUBSTANCES

The substances harmful to people with glutaric aciduria type I – glutaric acid and 3-hydroxyglutaric acid – are formed out of lysine and tryptophan.

LYSINE AND TRYPTOPHAN ARE ESSENTIAL AMINO ACIDS

Both amino acids belong to the group of essential (vital) amino acids. This means that they need to be taken in through food in sufficient quantities, because they cannot be synthesised by the body. Therefore, patients with glutaric aciduria type I have to take in small quantities of these amino acids through food.

LYSINE INTAKE ON A "NORMAL" DIET IS ABOUT TWICE AS HIGH AS REQUIRED

A 3-year-old child on a normal diet is supplied with about 2000 mg lysine a day. However, the actual requirement of a 3-year-old child is significantly lower, about 900 mg a day on average, i.e. 60 mg/kg body weight (BW).

RECOMMENDATIONS FOR LYSINE AND NUTRIENT INTAKE

Except for the amino acids lysine and tryptophan, the children are supplied with the same nutrients as children with a healthy metabolism.

Based on Table 2, the treatment centres regularly adapt the daily intake of lysine and amino acid supplement to the current body weight. This recommendation conforms to the current S3 guideline for glutaric aciduria type I (www.awmf.org).

However, the energy requirements vary between individuals as well as depending on age and level of physical activity. Therefore, the recommendations given in the table are merely intended as approximate reference values. Regular checks of body weight and growth show whether the selected intake actually matches the child's requirement. The energy and fluid requirements of patients with movement disorders are expected to be higher.

LOW-LYSINE AND LOW-TRYPTOPHAN DIET

The principle of the diet consists in limiting the lysine and tryptophan content in food to the amount needed by the body for protein synthesis and for age-appropriate growth and development. Lysine and tryptophan are contained in the nutrient protein, which is why the intake of these amino acids can only be reduced by restricting the protein intake (low-protein diet).

LYSINE REDUCTION IS MORE IMPORTANT THAN TRYPTOPHAN REDUCTION

The proportion of lysine in foods is much higher than that of tryptophan. The tryptophan intake is automatically reduced by reducing the lysine intake.

CALCULATING THE LYSINE CONTENT OF FOODS IS MORE ACCURATE THAN CALCULATING THE PROTEIN CONTENT

Targeted reduction of lysine intake by calculating the protein content alone is not possible, because the lysine content in food protein varies greatly between food groups. The lysine content in food protein is between 2 and 10%. This means that the lysine content of two different foods with the same protein content may vary considerably.

AMOUNT	FOOD	PROTEIN	LYSINE
65 g	white bread contain	5 g	122 mg
150 g	drinking milk contain	5 g	425 mg

EXAMPLE

SIGNIFICANCE OF THE AMINO ACID SUPPLEMENT

To ensure that the body is adequately supplied with all other protein building blocks despite the limited protein intake from natural foods, it is advisable to add an amino acid supplement to the diet. See chapter about amino acid supplement.

CHECKING THE DIET

The body weight and growth are monitored on a regular basis to determine whether the dietary treatment is adequate and successful. The measurement of plasma amino acid levels is used to assess whether the body is adequately supplied with all amino acids. The plasma concentration of lysine and other amino acids should always be within the normal range.

SIGNIFICANCE OF ARGININE FOR THE DIETARY TREATMENT

Arginine is a semiessential amino acid, which, in contrast to lysine, can be synthesised by the body. It is additionally taken in through food, with only 40% being absorbed by the intestines. Arginine "displaces" lysine at the blood-brain barrier, because both use the same "entrance door" (transporter) to the brain. This mechanism can theoretically be taken advantage of for the dietary treatment. In animal experiments, however, only high-dose oral administration of arginine, as an additional measure to the low-lysine diet, was observed to result in a noticeable further decrease in toxic metabolites in the brain. This has so far not been systematically studied in humans. Moreover, this may also cause health problems (arterial hypotension, headache, hypoglycaemia).

Similar to lysine, the arginine content in natural protein is subject to strong variations. The arginine content of lysine-free, tryptophan-reduced, arginine-fortified amino acid supplements that used to be commercially available in Germany still showed some differences in the first year of life, which are no longer present in currently available products. Hence, the arginine content is sufficient and all patients who received lysine-free, tryptophan-reduced, arginine-fortified amino acid supplements as part of a low-lysine therapy experience a positive effect on their neurological development.

PER KG AND DAY		0–6 M	7–12 M	1 Y	2 Y	3 Y	4–5 Y	AFTER 6 Y
LYSINE FROM NATURAL PROTEIN	mg	100	90	80	70	60	50–55	See[2]
SYNTHETIC PROTEIN FROM AAS	g	1,3–0,8	1,0–0,8	0,8	0,8	0,8	0,8	
ENERGY[1]	kcal	100–80	80	94–81	94–81	94–81	86–63	

TABLE 2

AAS = Lysine-free, tryptophan-reduced amino acid supplement, M = month, Y = year

[1] According to the recommendations given by D-A-CH (2015)

[2] After the age of 6 years, controlled protein intake according to the Optimix® recommendations[3], see Table 11, p. 40

[3] Optimix®, Research Institute for Child Nutrition, Dortmund; URL: http://www.fke-do-de/index.php

At present, there is no evidence that additional, high-dose supplementation of arginine as part of metabolic maintenance or emergency treatment provides any benefits. Arginine should therefore only be taken in through natural foods and the amino acid supplement.

AMINO ACID SUPPLEMENT

The lysine-free, tryptophan-reduced amino acid supplement (AAS) adds all amino acids to the dietary treatment – except for lysine. It is additionally enriched with the vitamins, minerals and trace elements contained in protein-rich foods. It is therefore an important addition to the low-lysine diet. The composition of all amino acids, vitamins, minerals and trace elements (micronutrients) is adapted to the age-appropriate requirements. A sufficient intake of these substances is indispensable for protein synthesis in the body and thus for age-appropriate growth as well as for many important functions of the body.

All AAS available on the market in Germany contain a small amount of tryptophan. The addition of this amino acid is to prevent the risk of tryptophan deficiency. Tryptophan deficiency can lead to severe neurological disorders. On regular intake of the amino acid supplement in the specified dose, combined with the foods recommended for the low-lysine diet, the body is supplied with all amino acids, including tryptophan, as well as all micronutrients in sufficient quantities.

DISTRIBUTION OF THE DAILY DOSE

The AAS dose should be divided into at least 3 doses, directly after or during meals. Only then is it possible to ensure that all amino acids are used by the body for protein synthesis. When taking the entire daily dose at once or on an empty stomach, the amino acids enter the bloodstream too quickly. Some of the amino acids are then used for energy metabolism instead of protein synthesis. The absorption of the micronutrients may be affected as well.

RECOMMENDATIONS FOR PREPARATION

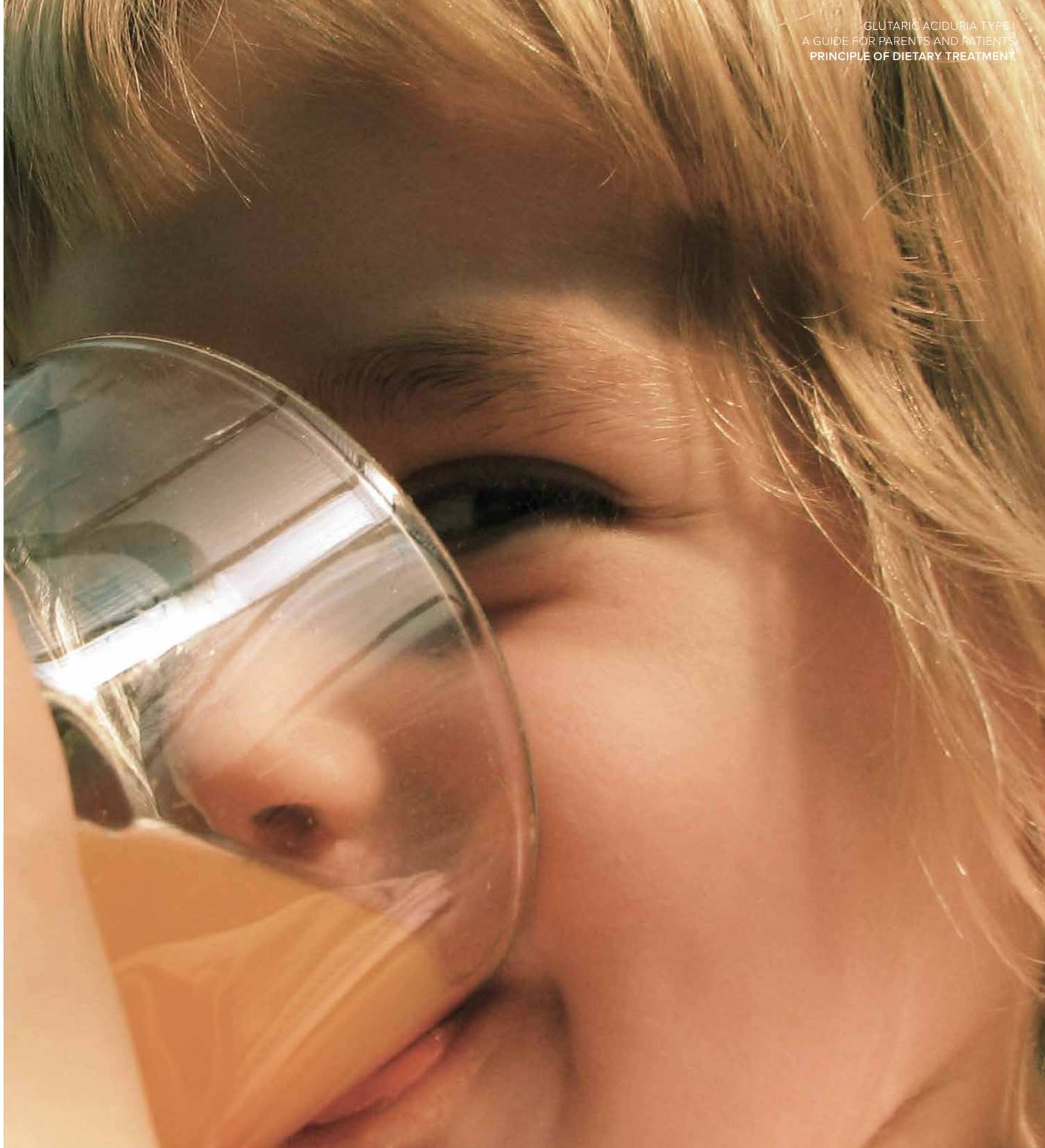
Amino acid supplements in powdered form can be prepared as a drink, cream or gel. The specified amount of liquid should be followed, because otherwise nausea, abdominal pain or diarrhoea may occur.

The powder can be mixed with less liquid if the missing liquid is drunk directly thereafter.

The following flavour carriers can be used:
— Tea, fruit or vegetable juice, fruit nectar, soft drinks
— Granulated tea or powdered drink mix
— Fruit syrup
— Sweet cream and vanilla sugar
— Vegan cereal-based milk substitute – no soya drink
— Fruit puree, e.g. apple puree
— Low-protein pudding
— Vegetable puree
— Tomato ketchup, tomato juice

TIPS FOR INTAKE

— Establish a regular daily ritual for intake after or during meals
— Treat as a medicine
— The taste is less intense if well chilled
— Be consistent in feeding and do not allow any exceptions, especially with toddlers
— Praising the child can make the intake easier



DIET FOR INFANTS

BREASTFEEDING

Infants with glutaric aciduria type I can also be breastfed. In this case, the amount of breast milk is reduced and replaced by a defined amount of lysine-free, tryptophan-reduced special formula.

The special formula is fed at the beginning of the meal. Thereafter, the infant can be breastfed until sated. Since the amount of breast milk and thus the lysine intake are estimated, regular monitoring of weight increase and growth, and measurement of plasma amino acid levels are necessary. This approach is a commonly used method that is considered to be safe.

However, if a precisely calculated daily lysine intake is specified, the amount of breast milk needs to be measured. The infant's milk intake is determined by weighing the infant before and after breastfeeding (test weighing). The results are recorded and added up over a period of 24 hours. The specified amount of breast milk is fed at the beginning of the meal, followed by the lysine-free, tryptophan-reduced special formula as needed.

CALCULATING THE AMOUNT OF LYSINE-FREE, TRYPTOPHAN-REDUCED SPECIAL FORMULA

Sufficient reduction of lysine intake is already achieved by reducing the daily intake of breast milk by about 20%. This means that the infant gets 20% of their usual drinking amount from the lysine-free, tryptophan-reduced special formula and 80% from breast milk.

The table below shows the proportion of special formula and breast milk in the total drinking amount in relation to the body weight.

WEIGHT (KG)	SPECIAL FORMULA (ML)	BREAST MILK ESTIMATED AMOUNT (ML)	TOTAL DRINKING AMOUNT ESTIMATED AMOUNT (ML)
3,0–3,5	100	400	500
3,6–4,0	120	450–500	600
4,1–4,5	140	550–600	700
4,6–5,5	160	600–650	800
5,6–6,0	180	700–750	900
> 6	200	800	1000

TABLE 4 **DOSAGE OF THE SPECIAL FORMULA**

Rule of thumb: An infant drinks roughly the amount corresponding to one-sixth of their body weight within 24 hours.

FEEDING BABY FORMULA

Infant formulas contain more lysine than breast milk, which is why the proportion of special formula is higher in non-breastfed infants. The specified daily lysine dose is reached by feeding a calculated amount of baby formula. The specified amount of baby formula is fed at the beginning of the meal, followed by the special formula as needed.

Once the baby formula is used up, exclusively special formula is fed at all other meals.

INTRODUCTION OF COMPLEMENTARY FOOD

Complementary food, including vegetable, cereal and fruit pap, should be introduced as in healthy infants according to the dietary plan of the Research Institute for Child Nutrition in Dortmund (www.fke-do.de). In this case, the food selection is adapted to the special dietary requirements in glutaric aciduria type I.

1st **step**: vegetable & potato pap at the age of 4–5 months
2nd **step**: low-protein “milk” & cereals pap at the age of 5–6 months
3rd **step**: fruit & cereals pap at the age of 6–7 months
4th **step**: bread at the age of 10–12 months

As soon as complementary feeding is started, the lysine content of the foods needs to be calculated. The amount of breast milk or baby formula is reduced accordingly.

TAKING THE AMINO ACID SUPPLEMENT IN INFANCY

On starting complementary feeding, an amino acid supplement has to be fed. Starting at such an early age is important for the infant to get used to the taste in time. Experience has shown that getting used to the taste at an early stage facilitates the infant's later acceptance of the amino acid supplement.

Initially, the amino acid supplement can be stirred into 1–2 spoons of pap. It should be fed during or after meals to ensure optimum usability of all ingredients. At the beginning, a small dose is given, which is adapted by the attending dietician or metabolic specialist over the course of time.

FOOD CLASSIFICATION

GROUP 1
SUITABLE FOODS

These foods contain relatively small amounts of lysine or are lysine-free. A daily lysine allowance can be calculated for these foods.

— **Selected cereals and cereal products**
Bread, baked goods without milk or eggs
Pasta without eggs
Rice
Flour, cereal flakes and semolina of: wheat, spelt, rye, maize, millet, rice

— **Vegetables up to 100 mg LYS/100 g**
e.g. tomatoes, cucumbers, carrots, kohlrabi, sweet pepper

— **Fruit up to 50 mg LYS/100 g**
e.g. apples, pears, strawberries, grapes, plums

— **Vegan milk substitute products**
e.g. drinks, yoghurt, cream or cheese substitute – not based on soya

— **Spreads with a protein content up to 3 g/100 g**

— **Vegetable oils, margarine, butter, lard**

— **All types of sugar, jam, jelly, honey, syrup**

— **Sweets without gelatin, milk, cocoa or nuts**

— **Desserts without gelatin and milk**
e.g. jelly, fruit ice cream, fruit pudding, fruit cream, puddings based on milk substitutes

— **Beverages**
e.g. water, tea, apple juice, fruit juice drinks, soft drinks

GROUP 2
FOODS WITH LIMITED SUITABILITY

These foods contain relatively large amounts of lysine and should therefore be calculated or weighed. For foods of this group, the lysine amount equivalent to the difference between the specified lysine intake and the daily lysine allowance is available.

— **Cereals and cereal products of oat and buckwheat**

— **Potatoes**

— **Vegetables above 100 mg LYS/100 g**
e.g. cauliflower, broccoli, spinach (no legumes)

— **Fruit above 50 mg LYS/100 g**
e.g. banana, kiwi, melon

— **Fruit juices above 15 mg LYS/100 g**
All pure juices except for apple juice

— **Spreads above 3 g protein/100 g**

— **Special low-protein or vegetarian sausage products**

— **Milk and dairy products**
e.g. drinking milk, yoghurt, cream, crème fraiche, clotted cream, double-cream cheese

— **Nuts and seeds up to 450 mg LYS/100 g**
e.g. coconut, macadamia nuts, walnuts, hazelnuts, sweet chestnuts, pecan nuts

— **Chocolate and sweets containing chocolate**

GROUP 3
UNSUITABLE FOODS

These foods are very rich in lysine and are therefore not suitable.

— **Meat, poultry**

— **Fish**

— **Eggs**

— **Cheese varieties below 60% FDM, low-fat quark**

— **Legumes, e.g. lentils, beans, chickpeas**

— **Nuts and seeds above 450 mg LYS/100 g**
e.g. almonds, peanuts, cashew nuts, Brazil nuts, pistachios, pumpkin seeds, pine nuts, sunflower seeds, linseeds, sesame seeds, poppyseeds, quinoa, amaranth

THE DAILY LYSINE ALLOWANCE

The so-called “daily lysine allowance” makes it easier to implement the diet in everyday life.

The average lysine content of the basic foods from the green group is calculated and referred to as the daily allowance. This is deducted from the specified daily lysine intake.

Weighing and calculating these foods, such as bread, pasta, low-lysine vegetable and fruit varieties, on a daily basis is thus not necessary. The daily allowance has to be checked at regular intervals to register any changes in consumption. The dietitian at your treatment centre will explain to you how to use this calculation method.

ESTIMATING THE LYSINE CONTENT IN FOOD PROTEIN

The approximate lysine content of convenience products can be determined by looking at the list of ingredients. The following information is needed for this method of calculation:

— Protein content of the convenience product
— Main protein source of the convenience product

Different protein sources have different lysine contents. The protein source is stated in the list of ingredients, where the ingredients of a convenience product are listed in descending order of their proportion by weight.

Depending on the composition of the food in question, the protein source is selected from the table below and the corresponding content in mg lysine per 1 g protein is read off. This figure is the factor by which the protein content of the convenience product is multiplied.

	FOOD	PROTEIN SOURCE	MG LYS/G PROTEIN
1	Bread, pasta, semolina, flakes, flour, pastry without milk[1] or egg	Wheat, spelt, millet, maize	30
2	Bread, pasta, flakes, flour, pastry without milk[1] or egg	Rye, oat, barley, rice	40
3	Cereal products and baked goods with low milk[1] and/or egg content, e.g. porridge, pastry and cake	Wheat, spelt, maize, millet, rye, oat, barley, rice, egg, milk[1]	45
4	Cereal products and baked goods with high milk[1] and/or egg content, e.g. pudding, pancakes, sponge	Milk[1], egg, wheat, spelt, maize, millet, rye, oat, barley, rice	60
5	Fruit, e.g. fruit juices, fruit ice cream, fruit pudding, jelly with gelatin	Fruit, gelatin	55
6	Vegetable products, e.g. vegetable sauces and soups, ketchup, without meat, egg or milk[1]	Vegetables	40
7	Vegetable products with milk[1] or egg	Vegetables, milk[1], eggs	60
8	Potato products, e.g. soups and sauces with milk[1] and/or egg, soya products	Potatoes, soya and other legumes, eggs, milk[1]	60
9	Milk[1] and all dairy products, baker's yeast	Milk[1], yeast	80
10	Milk chocolate	Cocoa, milk[1]	45
11	Meat and sausage	Meat	90
12	Fish and seafood	Fish, seafood	100

TABLE 5

[1] Milk means all dairy products, such as cheese, yoghurt, quark, skim milk, skim milk powder, etc. The figures are based on calculated average values from the Prodi 6.6 nutrient database (German Nutrient Database 3.02, Souci, Fachmann, Kraut 2015)

HOW MANY MG LYSINE ARE CONTAINED IN 100 G BUTTER SPRITZ BISCUITS?

The packaging should also state the protein content next to the list of ingredients.

Protein content
100 g butter spritz biscuits contain 5.4 g protein
Protein source
See list of ingredients

List of ingredients
Wheat flour, clarified butter, sugar, whole egg, salt

1.
Write down the protein content: 5.4 g protein (per 100 g butter spritz biscuits)

2.
Read off the corresponding protein source(s) from the list of ingredients on the packaging. Since wheat is listed first and whole egg is listed at the last but one position, wheat has a higher proportion by weight.

3.
Select in the table the combination of protein sources that most closely corresponds to the list of ingredients and read off the factor. In this case, this is line 3 with the factor 45.

4.
Calculate the lysine content (estimated value): This factor (45) is multiplied by the protein content of the biscuits.

45 mg lysine x 5.4 g protein
= 243 mg lysine

Result
100 g butter spritz biscuits contain 243 mg lysine.

PATIENTS WITH MOVEMENT DISORDERS

There are special recommendations for patients with movement disorders, who have increased nutrient requirements and difficulty eating or being fed. These children are exposed to an increased risk of malnutrition and failure to thrive, which can lead to significant and rapid deterioration of the nutritional condition, and increase the severity of movement disorders. For this reason, these children should be regularly monitored by the physician and the dietitian.

1. GENERAL RECOMMENDATIONS

— Regular monitoring of body weight and growth
— Ensure appropriate position of the child during feeding
— Pay attention to the increased fluid and energy requirements, depending on the severity of the dystonic movement disorder
— Consider tube-feeding (at night)

2. CHILDREN WITH MILD DIFFICULTIES IN CHEWING AND SWALLOWING

The following foods are suitable for feeding these children:
— Cereal, milk and fruit pap
— Pureed vegetables with potatoes, pasta or cereal flakes
— Muesli
— Soft bread
— Fruit-vegetable shakes (smoothies)
— Split the diet into smaller, more frequent meals; if necessary, introduce a late meal before bedtime

Depending on the child's specific energy requirements, the caloric content of the meals can be increased, for example using
— Maltodextrin
— High-quality vegetable oils or cream
— Protein-free formula

Dosage recommendations will be given by the dietitian at your treatment centre. You can use an immersion blender or a blender attachment for kitchen machines to mince the food.

3. CHILDREN WITH SEVERE FEEDING PROBLEMS

— See no. 2 for the recommended diet
— Prepare the food as concentrated as possible (many calories – small volume)
— Thicken beverages, if necessary
— Placement of a nasogastric tube or a percutaneous endoscopic gastrostomy (PEG) tube, if there is no improvement

4. FEEDING VIA THE NASOGASTRIC OR PEG TUBE

— Partial or complete tube-feeding is possible. Children who still enjoy eating can get “normal” meals during the day and be fed via the tube at night.
— The use of a nutritionally complete tube feeding formula is recommended. In most cases, however, energy supplements need to be used in addition.
— The composition of the tube feeding formula must be regularly checked as regards lysine intake and supply with all nutrients and energy.

EMERGENCY DIETARY TREATMENT AT HOME

(IN CONSULTATION WITH THE TREATMENT CENTRE)

If the total drinking amount indicated in the emergency treatment protocol is not reached, tea or water, enriched with grape sugar or maltodextrin, should be given about every 2 hours (see table maltodextrin solution).

GENERAL PROCEDURE

Reduce the lysine intake by at least 50%. Subsequently, increase the lysine intake stepwise until reaching the level of the normal dietary plan within 1–3 days.

Avoid lysine-rich foods, such as milk and dairy products, lysine-rich vegetable and fruit varieties (select food exclusively from the green group).

Continue feeding lysine-free, tryptophan-reduced amino acid supplement.

Enrich beverages with maltodextrin/grape sugar (see table maltodextrin solution).

The implementation of the emergency treatment can be facilitated by creating an individual emergency treatment protocol.

INFANTS

Infants can temporarily (i.e. for 24–48 h max.) be fed the lysine-free, tryptophan-reduced special formula instead of baby formula containing lysine. The special formula (formulated according to the individual emergency treatment protocol) should be fed at short intervals over a maximum period of 24–48 hours. The lysine intake should be increased starting from day 2 or day 3 at the latest.

Day 2: 50% of the daily lysine intake
Day 3: 70–100% of the daily lysine intake
Day 4: full daily lysine intake

CARNITINE

The carnitine dose is doubled for the duration of the emergency treatment.

AGE	MALTODEXTRIN SOLUTION	DAILY AMOUNT
YEARS	% Kcal/100 ml	ml
0–1	10–15 40–60	150–200/kg body weight
1–2	15 60	120/kg body weight
2–6	20 80	1200–1500
6–10	20 80	1500–2000
> 10	25 100	2000

TABLE 6 **MALTODEXTRIN SOLUTION IN THE EVENT OF ILLNESS**[1]
The information is expressed in percentage by volume, e.g. 100 g maltodextrin dissolved in 1000 ml water corresponds to a 10% solution.
[1] From: Dixon MA and Leonard JV. Intercurrent illness inborn errors of intermediary metabolism. Arch Dis Child 1992; 67: 1387-1391

EXAMPLE DIETARY PLANS

AGE: 1 MONTH – INFANT IS BREASTFED
Weight in kg: 3,40 | **Length**: 52 cm
Estimated drinking amount: approx. 500 ml | **Target**: 20% of the estimated drinking amount as special formula
100 ml LYS-free TRP-reduced special formula | **Lysine**: 100 mg/kg BW = 340 mg/day

	AMOUNT	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
BOTTLE WITH LYS-FREE TRP-REDUCED SPECIAL FORMULA divided into 6 meals	100 ml	0	2,0	3,5	7,5	70
BREAST MILK as needed	400 ml	344	4,4	16,0	28,0	276
IN TOTAL PER DAY		344	6,4	19,5	35,5	346
IN TOTAL PER DAY/KG BW		101	1,9	5,7	10,4	102
ENERGY IN %			7%	51%	42%	

TABLE 7
The specified amount of LYS-free TRP-reduced special formula is fed at the beginning of the meal, followed by breastfeeding as needed.

AGE: 3 MONTHS – INFANT IS FED BABY FORMULA
Weight in kg: 5,10 | **Length**: 60 cm
Target: 100 mg lysine/kg BW = 510 mg/day LYS-free TRP-reduced special formula as needed

	AMOUNT	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
BOTTLE WITH BABY FORMULA STAGE 1 OR PRE 6 x 70 ml	420 ml	512	5,5	13,9	31,5	277
LYS-FREE TRP-REDUCED SPECIAL FORMULA as needed	300 ml	0	6,0	10,5	22,5	210
IN TOTAL PER DAY		512	11,5	24,4	54,0	487
IN TOTAL PER DAY/KG BW		100	2,2	4,8	10,6	95
ENERGY IN %			9%	47%	44%	

TABLE 8
The specified amount of baby formula is fed at the beginning of the meal, followed by the special formula as needed. Specifying a minimum drinking amount is only necessary in the event of insufficient weight increase.

AGE: 8 MONTHS
Weight in kg: 8,50 | **Length**: 72 cm
Estimated drinking amount: approx. 500 ml | **Target**: lysine: 90 mg/kg BW = 760–800 mg/day
Protein from amino acid supplement (AAS)/kg BW: 0,8–1 g = 7–9 g in total

	AMOUNT	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
BOTTLE WITH BABY FORMULA STAGE 1 OR PRE	150 ml	183	2,0	5,0	11,3	99
LYS-FREE TRP-REDUCED SPECIAL FORMULA as needed	50 ml	0	1,0	1,75	3,75	35
VEGETABLE MEAL						
E.G. PASTA IN BROCCOLI CREAM SAUCE	220 g	271	4,6	4,6	17,2	134
BUTTER OR OIL approx. 1 tsp	5 g	0	0	5	0	45
LYS-FREE TRP-REDUCED AAS (with 50 g protein/100 g) stirred into 1–2 spoons of pap	5 g	0	2,5	0	1,1	15
FRUIT & CEREAL PAP						
FRUIT PAP, as needed	150 g	36	0,8	0,2	22,5	74
RUSK	20 g	39	2	0,9	14,6	77
BUTTER OR OIL approx. 1 tsp	5 g	0	0	5	0	45
LYS-FREE TRP-REDUCED AAS (see above) stirred into 1–2 spoons of pap	5 g	0	2,5	0	1,1	15
MILK & CEREAL PAP						
BABY FORMULA STAGE 1 OR PRE	150 ml	183	2,0	5,0	11,3	99
LYS-FREE TRP-REDUCED SPECIAL FORMULA	50 ml	0	1,0	1,75	3,75	35
RICE FLAKES OR SEMOLINA	20 g	44	1,4	0,2	17,3	77
PEAR	20 g	5	0,1	0,1	2,5	12
LYS-FREE TRP-REDUCED AAS (see above) stirred into 1–2 spoons of pap	5 g	0	2,5	0	1,1	15
Additional liquid approx. 100 ml						
IN TOTAL PER DAY		761	22,3	29,4	107,5	776
IN TOTAL PER DAY/KG BW		90	2,6	3,5	12,6	91
ENERGY IN %			11%	34%	55%	

TABLE 9

Foods that are included in the daily lysine allowance

Foods that are calculated and weighed

AGE: 3 YEARS
Weight: 15 kg | **Height**: 100 cm
Target: 60 mg lysine/kg BW = 900 mg/day | Protein from amino acid supplement (AAS)/kg BW = 0,8 g protein = 12 g protein from AAS

AMOUNT	INGREDIENTS	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
	BREAKFAST					
40 g	WHEAT-RYE BREAD	96	3,4	1	19	98
1,5 TL	BUTTER	4	0,1	6	0	56
2 TL	JAM	1	0,0	0	7	28
40 g	GRAPES	6	0,3	0	6	29
80 ml	COW MILK 3.5% FAT	226	2,7	3	4	52
7 g	LYS-FREE TRP-REDUCED AAS		4,2		1	21
60 ml	APPLE JUICE	3	0,0		7	28
	SUBTOTAL	**336**	**10,7**	**10**	**43**	**312**
	LUNCH					
100 g	PASTA, COOKED, WEIGHED	96	5,0	0	28	143
80 g	TOMATO	29	0,8	0	2	16
50 g	COURGETTE	67	1,0	0	1	12
10 g	CREAM 30% FAT	17	0,2	3	0	30
2 TL	COLZA OIL (RAPESEED OIL)	0	0,0	10	0	88
7 g	LYS-FREE TRP-REDUCED AAS		4,2		1	21
60 ml	APPLE JUICE	3	0,0		7	28
	SUBTOTAL	**336**	**10,7**	**10**	**43**	**312**
	SNACK					
40 g	PEAR	10	0,2	0	5	23
30 g	YEAST CROISSANT	72	2,2	2	15	91
1,5 TL	BUTTER	4	0,1	6	0	56
	SUBTOTAL	**86**	**2,5**	**9**	**20**	**169**
	DINNER					
40 g	WHEAT-RYE BREAD	96	3,4	1	19	98
1 TL	BUTTER	2	0,0	4	0	37
20 g	CREAM CHEESE MIN. 70% FDM	145	1,9	7	1	75
60 g	RAW APPLES AND CARROTS	23	0,4	5	6	73
7 g	LYS-FREE TRP-REDUCED AAS		4,2		1	21
60 ml	APPLE JUICE	3	0,0		7	28
	SUBTOTAL	**269**	**10,0**	**17**	**32**	**332**
	BEVERAGES					
300 ml	WATER, TEA	0	0,0	0	0	0
100 ml	APPLE JUICE	5	0,1		11	47
	SUBTOTAL	**5**	**0,1**	**0**	**11**	**47**
	TOTAL PER DAY	**907**	**34,6**	**50**	**145**	**1198**
	TOTAL PER DAY/KG BW	**60**	**2,3**	**3,3**	**9,7**	**80**
	ENERGY IN %		**12**	**37**	**51**	

TABLE 10

DIET AFTER THE AGE OF 6 YEARS

RECOMMENDED CONSUMPTION AMOUNTS

The diet is based on the recommendations of Optimix® (optimised mixed diet), a concept for a healthy diet for children and adolescents. Optimix® was developed by the Research Institute for Child Nutrition (FKE) in Dortmund. www.fke-do.de

In this age group, the basic foods are cereals and cereal products as well as fruit and vegetables, supplemented with a limited amount of animal products.

The amounts of animal products indicated in the table below are classified by age groups. They are considered to be the framework for a protein-controlled diet. When following these indicated amounts, the body is supplied with all important nutrients in sufficient quantities.

ANIMAL PRODUCTS	RECOMMENDED CONSUMPTION AMOUNT	6 Y	7–9 Y	10–12 Y	13–14 Y	15–18 Y
MILK, DAIRY PRODUCTS[1]	ml/day, g/day	350	400	420	425 (f) 450 (m)	450 (f) 500 (m)
MEAT, SAUSAGE	g/day	40	50	60	65 (f) 75 (m)	75 (f) 85 (m)
EGGS	piece/week	2	2	2–3	2–3 (f/m)	2–3 (f/m)
FISCH	g/week	50	75	90	100 (f/m)	100 (f/m)

TABLE 11
Average recommended consumption amounts of animal products for school children and adolescents according to Optimix® f = female; m = male
[1] 100 ml milk can be replaced with approx. 15 g semi-hard cheese

FOOD SELECTION (AFTER THE AGE OF 6 YEARS)

SUITABLE

— **Cereals and cereal products**
Bread, pasta, rice, baked goods without lysine-rich nuts and seeds
— **Potatoes prepared in any way**
— **Vegetables except for legumes**
— **Fruit**
— **Cooking and spreadable fat**
Butter, margarine, vegetable oils, lard
— **Cream, crème fraiche**
— **Seeds and nuts up to 450 mg LYS/100 g**
Coconut, macadamia nuts, walnuts, hazelnuts, pecan nuts, sweet chestnuts
— **Sugar and foods containing sugar**
Jam, jelly, honey, syrup, sweets, sweets containing chocolate – preferably without lysine-rich nuts and seeds

LIMITED SUITABILITY
(see Table 11 for amounts)

— **Milk and dairy products**
e.g. yoghurt, cheese with more than 30% fat content
— **Egg**
— **Meat, sausage**
— **Fish**
— **Legumes**
(100–150 g per week, cooked)
— **Nuts and seeds up to 800 mg LYS/100 g**
e.g. almonds, Brazil nuts, sesame seeds

The foods of the yellow group are needed for a sufficient supply of high-quality proteins, minerals, vitamins and trace elements. Milk and dairy products should be preferred over meat and sausage.

UNSUITABLE

— **Nuts and seeds above 800 mg LYS/100 g**
Peanuts, cashew nuts, pistachios, pumpkin seeds, sunflower seeds, poppyseeds, linseeds, pine nuts
— **Fish, meat and sausage**
Larger amounts than indicated in the table
— **Legumes**
Larger amounts of lentils, broad beans, soya beans, peas, chickpeas

AGE: 6 YEARS
Weight: 20 kg I **Height**: 119 cm
Protein intake according to the consumption amounts recommended for a balanced diet by the Research Institute for Child Nutrition (Optimix®)

AMOUNT	INGREDIENTS	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
	BREAKFAST					
150 ml	ORANGE JUICE	13	1,0	0	13	65
	MUESLI OF:					
40 g	MUESLI MIX	139	4,1	2	24	141
5 g	COCONUT FLAKES	15	0,4	3	0	33
100 g	BERRIES	38	0,8	0	6	36
100 g	FRUIT YOGHURT 3,5% FAT	279	3,9	3	15	106
	SUBTOTAL	**484**	**10,3**	**9**	**58**	**381**
	SNACK					
50 g	WHOLEMEAL ROLL	116	4,2	1	21	116
10 g	BUTTER	5	0,1	8	0	74
15 g	SALAMI	248	2,9	5	0	56
40 g	CUCUMBER	11	0,2	0	1	6
	SUBTOTAL	**380**	**7,4**	**14**	**22**	**252**
	LUNCH					
160 g	PASTA, COOKED, WEIGHED	154	8,0	1	45	229
10 g	OLIVE OIL	0	0,0	10	0	88
5 g	ONIONS	3	0,1	0	0	2
5 g	TOMATO PASTE	5	0,1	0	0	2
50 g	BUTTON MUSHROOMS	85	2,1	0	0	12
100 g	TOMATO	36	1,0	0	3	20
40 ml	VEGETABLE BROTH	4	0,1	1	0	8
	SUBTOTAL	**287**	**11,3**	**12**	**49**	**361**
	SNACK					
100 g	FRUIT	19	0,3	0	14	65
20 g	CHOCOLATE BAR	72	1,3	4	13	96
	SUBTOTAL	**91**	**1,7**	**4**	**28**	**161**
	DINNER					
50 g	WHEAT-RYE BREAD	120	4,3	1	23	123
10 g	BUTTER	5	0,1	8	0	74
15 g	SEMI-HARD CHEESE MIN. 45% FDM	235	3,1	3	0	44
30 g	SWEET PEPPER	18	0,3	0	1	7
150 ml	COW MILK 3,5% FAT	425	5,1	5	7	98
	SUBTOTAL	**802**	**12,9**	**18**	**31**	**345**
	BEVERAGES					
700 ml	WATER, TEA	0	0,0	0	0	0
	TOTAL PER DAY	**2045**	**43,5**	**57**	**188**	**1500**
	TOTAL PER DAY/KG BW	**102**	**2,2**	**2,9**	**9,4**	**75**
	ENERGY IN %		**12**	**34**	**54**	

TABLE 12

FOOD COMPOSITION AND NUTRITION TABLE FOR CALCULATING THE LYSINE CONTENT

ALL NUTRITIONAL INFORMATION GIVEN REFERS TO 100 G OF THE FOODS LISTED

Source: Prodi 6.6 Expert (German Nutrient Database 3.02, SOUCI FACHMANN KRAUT 2015)

FOOD	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
BAKED GOODS					
Apple pie of shortcrust pastry	93	2,9	9	35	233
Apple strudel	64	2,3	6	26	171
Berliner filled with cherry jam	236	6,2	11	46	310
Black-and-white cookie of cake batter	213	5,1	11	50	320
Braided yeast bun of yeast dough	270	7,8	1	52	257
Brioche without filling	303	7,5	11	36	273
Butter cookies of shortcrust pastry	192	6,3	25	60	502
Butter croissant of yeast dough, e.g. German sweet bread	240	7,5	8	49	302
Cake of cake batter, e.g. marble cake, pound cake, muffins	242	6,4	15	48	365
Cheesecake	610	9,1	9	23	216
Croissant of puff pastry	233	7,5	33	45	514
Flan case of sponge mixture	335	7,6	11	48	322
Honey cake	135	4,4	1	68	310
Meringue	321	5,6	0	84	364
Pig's ears of puff pastry	110	5,6	30	53	505
Puff pastry	98	4,1	32	29	422
Rusk	195	9,9	4	73	385
Shortbread	308	8,1	11	75	441
Sponge fingers	588	11,8	7	74	412
Sponge roll with lemon	255	4,7	9	30	221
Sweet dumplings of yeast dough	213	6,5	14	50	354
BAKING INGREDIENTS					
Baker's yeast, pressed, fresh, yeast cube	1230	16,7	1	1	96
Cocoa powder, slightly de-oiled	720	22,6	20	18	390
Dry yeast	2894	35,6	2	32	328
Gelatin	3800	84,2	0	0	343
Baking powder, baking soda, cream of tartar, cream stiffener, custard powder, etc. not calculated					
BREAD					
Crispbread	338	11,0	2	68	356
Flatbread	188	8,2	1	49	248
Granary bread	200	8,4	1	40	220
Lye pretzel/Pretzel stick	181	9,1	4	56	307
Roll/Baguette	190	8,9	2	56	278
Rye roll	299	8,0	2	39	226
Rye-wheat bread	300	6,7	1	46	230
Wheat-rye bread	209	7,4	1	46	236
White bread/Toast	188	8,2	1	49	248
Whole-wheat toast	213	7,9	3	48	262
Wholemeal bread	297	7,3	1	39	213
Wholemeal/Multi-grain roll	253	8,3	1	51	267
SPREADS					
Clotted cream 22% fat	200	2,8	22	4	220
Hazelnut spread, sweet	181	4,3	31	58	537
Honey	17	0,4	0	75	306
Jam, jelly, marmalade	7	0,1	0	69	284
Maple syrup	0	0,0	0	67	274
Sugar beet syrup	79	1,2	0	67	278
EGG					
1 chicken egg size M (approx. 58 g)	409	6,9	5	1	79
Chicken egg white	638	11,1	0	1	48
Chicken egg yolk	1123	16,1	32	0	348
Chicken egg	706	11,9	9	2	137
DELICATESSEN PRODUCTS					
Broth, granulated, dried product	1049	17,0	4	11	149
Capers, tinned, drained	140	2,1	0	3	28
Mayonnaise 80% fat	98	1,5	83	2	743
Meat broth, prepared	22	0,4	0	0	3
Mustard	362	6,0	4	6	88
Remoulade 65% fat	72	1,1	65	15	642
Soya sauce, convenience product	588	8,7	0	8	70
Tomato ketchup	94	2,1	0	24	112
Tomato paste	103	2,3	1	6	43
Vegetable broth, prepared	11	0,2	2	0	20
Vinegar (cider, aromatic, wine, etc.)	19	0,4	0	1	20
FATS AND OILS					
Butter	48	0,7	83	1	741
Clarified butter	18	0,3	100	0	880
Lard	9	0,1	100	0	882
Margarine	15	0,2	80	0	709
Vegetable oils, e.g. sunflower oil, rapeseed oil, olive oil, etc.	0	0,0	100	0	884
FISH AND SEAFOOD					
Crustaceans, cooked	1468	18,6	2	1	92
Fish fingers, breaded, deep-frozen	1033	12,1	9	14	183
Fish, cooked	2207	22,2	3	0	114
Fish, raw	1923	19,3	2	0	100
Mussels	842	10,5	1	3	66
Squid rings in batter, fried	1296	14,6	4	9	134
MEAT/SAUSAGE					

FOOD	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
Bavarian meat and pork loaf	1019	11,8	27	0	292
Bratwurst	1110	12,8	27	0	289
Chasseur sausage	1320	15,3	16	0	203
Chicken, raw	1768	19,9	10	0	166
Ham sausage	1437	16,6	10	3	172
Liver sausage	963	12,5	31	1	331
Meat (pork, beef, veal, lamb), cooked	2472	27,5	266	0	17
Meat (pork, beef, veal, lamb), raw	1843	20,5	14	0	207
Minced meat, half and half (beef/pork), raw	1723	19,4	16	0	224
Pork and veal sausage	920	11,6	28	0	293
Pork ham, cooked	2320	22,5	4	1	128
Pork ham, smoked, raw (leg)	1878	21,2	6	0	136
Pork sausage/Bologna sausage	930	12,1	28	0	300
Salami	1650	19,4	33	2	375
Sausage spread	1033	12,0	45	2	456
Sausage/Bockwurst/Wiener	1138	13,1	25	0	271
Turkey breast, raw	2110	24,1	1	0	107
VEGETABLES					
Artichoke	158	2,4	0	3	43
Asparagus	92	1,4	0	2	54
Aubergine	34	1,2	0	2	20
Beans, green	140	2,4	0	5	37
Beetroot	250	4,5	0	3	44
Black salsify	71	1,5	0	1	21
Broccoli	150	3,8	0	3	34
Brussel sprouts	95	1,6	0	2	18
Carrot	68	1,2	1	9	53
Cauliflower	140	2,5	0	2	28
Celeriac	363	6,0	0	28	145
Celery	19	1,2	0	2	21
Chard	189	3,1	1	2	35
Chicory	42	1,2	0	2	20
Chinese cabbage	58	1,1	0	1	16
Courgette	92	2,8	0	3	32
Cucumber	240	4,3	1	3	45
Dandelion	53	1,1	0	5	29
Endive	105	1,8	0	1	18
Garden lettuce	48	1,2	0	6	36
Garlic	47	0,8	0	7	39
Ginger tuber	26	0,6	0	2	14

FOOD	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
Horseradish	84	2,1	0	1	21
Iceberg lettuce	59	1,0	0	2	15
Kale	82	1,3	0	6	34
Kohlrabi	74	1,6	0	2	27
Lamb's lettuce	110	1,8	0	1	18
Leaf spinach	160	2,8	0	1	22
Leek	113	2,9	0	6	48
Okra	123	2,8	0	12	78
Olives black, pickled, drained	51	1,4	14	2	148
Olives green, pickled, drained	125	2,1	0	2	29
Onions	130	3,3	1	16	95
Parsnip	59	1,1	0	3	23
Peas, green	610	6,5	0	12	91
Pumpkin	70	1,2	0	1	14
Purslane	139	2,1	0	3	29
Radicchio	92	1,5	0	1	17
Radish	71	1,1	0	2	17
Red cabbage	82	1,5	0	8	47
Rocket	71	1,5	0	4	27
Romaine lettuce	58	1,1	0	2	18
Root parsley	78	1,3	0	12	64
Sauerkraut, drained	196	3,2	0	1	26
Savoy cabbage	65	1,4	0	4	30
Small radish	71	1,2	0	2	16
Sorrel	18	2,6	1	2	30
Spring onion/Green onion	92	1,4	0	3	23
Stinging nettle	415	7,4	1	1	48
Swede	64	1,9	0	4	28
Sweet maize	133	2,0	0	2	23
Sweet pepper	65	1,8	17	4	200
Tomato	89	2,0	0	2	21
White cabbage	51	1,0	0	5	32
Wild turnip/May turnip	29	0,9	0	3	20
CEREALS, CEREAL FLAKES, FLOURS					
Amaranth, raw	747	14,5	7	66	403
Arrowroot flour (maranta starch)	20	0,4	0	94	388
Barley, raw	377	11,2	2	63	338
Breadcrumbs	276	10,1	2	74	368
Buckwheat flour	305	5,1	1	78	351
Buckwheat groats, raw	390	8,1	2	73	348

FOOD	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
Cornflakes	180	7,7	1	80	368
Couscous, raw	319	11,7	2	69	353
Green spelt flour	284	10,4	2	77	383
Green spelt/Spelt raw	316	11,6	3	63	347
Maize semolina, polenta, raw	237	8,8	1	74	354
Maize starch	11	0,4	0	86	353
Millet flakes	240	10,6	4	69	364
Millet, whole grains, raw	226	9,6	4	64	355
Muesli without nuts and seeds	371	11,0	7	59	364
Oat, raw	440	10,7	7	56	351
Pearl barley, raw	320	10,4	1	71	351
Potato starch flour	41	0,6	0	83	341
Quinoa, raw	860	12,2	6	62	369
Rice, peeled, cooked	77	2,1	0	19	87
Rice, raw	270	7,4	1	78	355
Rye flour type 1150	350	9,0	1	68	338
Rye, raw	375	9,5	2	61	326
Wheat flakes	316	11,4	2	60	330
Wheat flour type 1050	300	12,1	2	67	347
Wheat flour type 405	211	10,0	1	72	348
Wheat semolina	281	10,3	1	69	342
Wheat starch	9	0,4	0	86	355
Wheat, raw	316	11,4	2	60	330
Wholemeal oat flakes	457	13,2	7	60	373
LEGUMES					
Beans white, raw	1694	21,3	2	40	277
Beans white, ripe, tinned, drained	715	9,0	1	17	117
Chickpeas, ripe, raw	1402	19,8	3	38	309
Chickpeas, tinned, drained	516	7,3	3	17	133
Kidney beans, raw	1768	22,1	1	37	292
Kidney beans, tinned, drained	750	9,4	1	15	124
Lentils, ripe, raw	1731	23,5	1	49	329
Peas, ripe, raw	1613	22,9	1	42	309
Soya beans, ripe, raw	1937	33,7	18	6	365
POTATOES, POTATO PRODUCTS AND HIGH-STARCH FOODS					
Batata (sweet potato)	70	1,6	1	24	117
Chips, ready-to-eat	275	4,2	15	36	295
Finger-shaped potato dumplings, raw	231	4,8	2	23	131
Fried potatoes, potato fritters, potato pancakes, fried/ready-to-eat	189	2,9	8	26	190
Gnocchi, raw	167	3,9	1	34	165
Jerusalem artichoke, raw	122	2,4	0	4	54
Plantain	69	1,1	0	28	127
Potato crisps	400	5,5	39	45	562
Potato croquettes	167	2,9	5	16	123
Potatoes, peeled, raw	127	1,9	0	16	76
CHEESE					
Blue mould cheese, min. 50% FDM, e.g. Roquefort	1628	21,6	30	1	358
Brie, min. 60% FDM	1199	16,8	33	0	362
Cheese spread, min. 50% FDM	904	12,0	27	7	318
Cooking cheese, min. 40% FDM	904	12,0	14	3	187
Cottage cheese	927	12,3	4	3	104
Double-cream cheese, min. 60% FDM	1200	11,3	32	3	337
Goat's cheese, min. 45% FDM	2012	25,3	27	0	344
Mascarpone, min. 80% FDM	390	4,5	40	3	387
Mozzarella of cow milk, min. 45% FDM	1440	17,1	21	2	263
Parmesan, min. 40% FDM	2447	34,3	30	0	407
Quark, min. 20% FDM	1050	12,5	5	3	109
Quark, min. 40% FDM	930	11,1	11	3	159
Raclette cheese, min. 45% FDM	1620	22,7	28	0	343
Semi-hard cheese, min. 30% FDM	2107	26,5	16	0	252
Semi-hard cheese, min. 45% FDM	2012	25,3	27	0	344
Semi-hard cheese, min. 50% FDM	1649	21,9	30	0	356
Sheep's cheese/Feta, min. 50% FDM	1204	15,7	24	1	284
HERBS					
Basil, fresh	204	3,1	1	5	47
Chives, fresh	192	3,6	1	2	40
Cress, fresh	321	4,2	1	2	41
Dill, fresh	243	3,7	1	8	65
Parsley leaf, fresh	280	4,4	0	7	60
Ramson, fresh	57	0,9	0	3	23
Sage, fresh	113	1,7	2	7	59
MILK AND DAIRY PRODUCTS					
Breastmilk	86	1,1	4	7	69
Buttermilk	330	3,5	1	4	37
Cow milk 3.5% fat	283	3,4	4	5	65
Cream 30% fat	168	2,4	32	3	303
Crème fraiche/Sour cream 40% fat	150	2,1	40	2	373
Fruit yoghurt 3.5% fat	279	3,9	3	15	106
Kefir 3.5% fat	230	3,2	4	4	64

FOOD	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
Sour cream 10% fat	200	2,8	18	3	187
Soured milk 3.5% fat	242	3,4	4	4	64
Soured milk with fruit	206	2,9	3	14	99
Sweet whey	79	0,8	0	5	25
Yoghurt 10% fat	221	3,1	10	4	118
Yoghurt 3.5% fat	280	3,9	4	4	69
PASTA/PASTA PRODUCTS					
Pasta, egg-free, of durum wheat semolina, cooked	107	5,6	1	31	159
Pasta, egg-free, of durum wheat semolina, raw	240	12,5	1	70	357
Wholemeal pasta products, egg-free, of wheat, cooked	163	6,0	1	27	153
Wholemeal pasta products, egg-free, of wheat, raw	366	13,4	3	61	345
NUTS AND SEEDS					
Almonds, sweet	580	24,0	53	6	611
Brazil nuts	530	17,0	68	4	697
Cashew nuts	1000	21,0	47	22	598
Coconut flakes	300	7,4	65	8	668
Hazelnuts	450	16,3	63	6	664
Linseeds	880	22,3	37	8	488
Macadamia nuts	336	8,8	73	4	719
Peanuts	1100	29,8	48	7	599
Pecan nuts	441	11,0	72	4	717
Pine nuts	868	24,0	51	7	589
Pistachios	1108	20,8	52	12	608
Poppyseeds	1195	23,8	42	4	526
Pumpkin seeds	2283	35,5	46	3	581
Sesame seeds	640	20,9	50	10	593
Sunflower seeds	960	26,1	26	35	491
Sweet chestnuts	150	2,9	2	41	212
Walnuts	410	16,1	71	6	723
FRUIT					
Apple	15	0,3	0	14	65
Apricot	69	0,9	0	9	45
Avocado	90	1,4	13	4	138
Banana	57	1,1	0	20	93
Blackberry	38	1,2	1	6	43
Blueberry	16	0,6	1	6	46
Cherries	36	0,9	0	13	64
Clementine	41	0,7	0	9	50
Cranberry	11	0,3	1	6	41

FOOD	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
Currants	36	1,1	0	5	40
Date	90	2,0	1	65	297
Fig, dried	140	3,5	1	55	272
Fig	60	1,3	1	13	67
Gooseberry	25	0,8	0	7	43
Grapefruit	19	0,6	0	7	45
Grapes	15	0,7	0	15	72
Honeydew melon/Muskmelon	67	0,9	0	12	57
Kaki	42	0,6	0	16	76
Kiwi	76	1,0	1	9	62
Lemon	35	0,7	1	3	39
Lime	31	0,5	2	2	48
Litchi	68	0,9	0	17	78
Mandarin	36	0,7	0	10	54
Mango	58	0,6	0	12	62
Mirabelle	24	0,7	0	14	67
Nectarine	44	0,9	0	12	60
Orange	39	1,0	0	8	47
Papaya	52	0,5	0	7	36
Passion fruit	182	2,4	0	10	67
Peach	29	0,8	0	9	44
Pear	26	0,5	0	12	58
Pineapple	35	0,5	0	12	59
Plums	19	0,6	0	10	48
Pomegranate	53	0,7	1	16	80
Quince	23	0,4	1	7	50
Raisins	71	2,5	1	68	314
Raspberry	42	1,3	0	5	43
Rhubarb	25	0,6	0	1	20
Strawberry	34	0,8	0	6	36
Watermelon	89	0,6	0	8	39
MUSHROOMS					
Birch bolete, raw	41	4,7	1	0	38
Button mushroom, raw	170	4,1	0	1	24
Cep, raw	190	5,4	0	1	39
Chanterelle, raw	39	2,4	0	0	21
Honey mushroom, raw	215	3,2	1	0	30
Morel, raw	168	2,5	0	1	28
Oyster mushroom, raw	150	3,5	0	3	35
Red bolete	98	2,2	1	0	26
Red pine mushroom, raw	57	2,8	1	0	28

FOOD	LYS (MG)	PROTEIN (G)	FAT (G)	CH (G)	CALORIES
Shiitake, raw	56	1,6	0	12	46
Truffle, raw	490	8,3	1	7	90
SPROUTS					
Bamboo sprouts, raw	128	2,5	0	1	23
Bamboo sprouts, tinned, drained	113	2,2	19	1	0
Lucerne sprouts (alfalfa), raw	224	4,0	1	2	35
Mung bean sprouts	246	3,2	0	2	26
Soya bean sprouts, raw	444	6,3	1	5	59
SWEETS, ICE CREAM, SNACKS					
Brittle	94	3,3	13	81	457
Candies	33	0,5	0	95	391
Chewing gum	7	0,1	0	95	387
Chocolate beans	215	4,6	4	78	381
Chocolate biscuits	222	6,7	24	55	466
Chocolate marshmallows	216[1]	3,6	11	64	357
Chocolate sprinkles	335	7,2	18	62	458
Crackers	218	11,1	3	75	386
Fondant	0	0,0	0	88	357
Fruit ice cream	107	1,5	2	29	142
Gummi bears with gelatin	434	6,6	0	79	348
Gummi bears without gelatin	0	0,1	0	83	334
Ice pop/Ice cream with artificial flavours and colourings	0	0,0	0	15	61
Jelly fruits	71	1,6	0	79	352
Liquorice	105	4,4	1	87	381
Marshmallows	132	2,0	0	80	333
Milk chocolate, with nuts	553	9,2	32	50	531
Milk chocolate	393	9,2	32	54	539
Milk ice	116	1,6	22	12	250
Peanut puffs	335	10,4	35	45	538
Popcorn	342	12,7	5	67	388
Potato crisps	400	5,5	39	45	562
Pretzel sticks	185	9,7	1	76	354
Puffed rice	291	7,5	2	84	394
Semisweet chocolate	377	8,1	31	46	514
Shortbread	308	8,1	11	75	441
Sorbet	12	0,2	0	32	139

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— Arbeitsgemeinschaft für Pädiatrische Stoffwechselstörungen e.V. (APS) in der Gesellschaft für Kinder- und Jugendmedizin (DGKJ): www.aps-med.de
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