Information for the U.S. products. Please refer to the Canadian product label for the list of ingredients and nutritional information for products available in Canada.

A GUIDE FOR FAMILIES WHO HAVE A CHILD WITH

Disorders of Leucine Catabolism

CONTENTS

Abbott provides this booklet to health care professionals to help them counsel families, and to families to help them learn about disorders of leucine catabolism.

INTRODUCTION TO DISORDERS OF LEUCINE CATABOLISM

Your child has been diagnosed with a *disorder of leucine catabolism* (lu-seen ka-tab-o-lism), or DLC for short. Children who have inherited this condition cannot use the essential amino acid leucine (lu-seen) (LEU) in a normal way. LEU is found in all foods that contain protein. You will need to feed your child all the foods necessary for normal growth and development, but only the amount of LEU he can safely use.

Learning some medical terms in nutrition and genetics will help you understand and manage your child's diet better. If you have any questions, write them down and ask the nutritionist (dietitian), nurse, or doctor at the metabolic clinic.

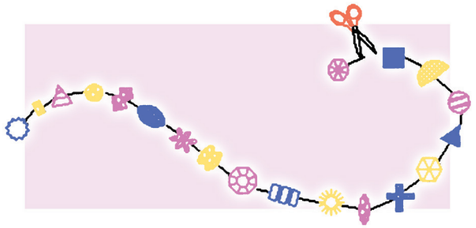


Figure 1. Amino acids are joined together like beads on a necklace to form protein. Enzymes act like scissors to remove amino acids from protein.

WHAT IS DLC?

A DLC is an inherited disorder of amino acid metabolism. Proteins, which are made up of amino acids, are found in many parts of the human body, including hair, blood, skin, and muscles. Most foods contain protein. When we eat foods containing protein, this protein is split into amino acids during digestion. The amino acids are later put back together, like beads on a necklace, to form new protein. These new proteins are used to build and repair the body's tissues.

Twenty amino acids occur commonly in the human body and in the foods we eat. LEU is one of these amino acids. LEU is an essential amino acid that is important for growth. All foods with protein contain LEU. High-protein foods include dairy products, beans and peas, eggs, fish and seafood, meat, poultry, nuts, soy products, seeds, and nut butters. Fruits, grains, and vegetables have less protein and, therefore, have less LEU. These are allowed in the diet in measured quantities.

Splitting protein into amino acids requires a special substance that does the actual work. Think of the splitting substance as a pair of scissors snipping beads off a necklace (Figure 1). The "scissors" are called enzymes (n-simes).

Once LEU is split off from food protein, it is absorbed, changed, and used to form many other useful substances in the body. In a DLC, the enzymes needed to rid the body of the products of the breakdown of LEU are absent or not working properly. People with a DLC, such as your child, do not have any normally working enzyme or do not have enough to handle all the LEU that is in the protein foods they eat. In either case, LEU cannot be used normally and LEU or the products from its breakdown build up as organic acid and other toxic (poisonous) substances.

This excess keeps another important substance, coenzyme A (CoA), from working and causes the symptoms of a disorder of leucine catabolism (Figure 2).

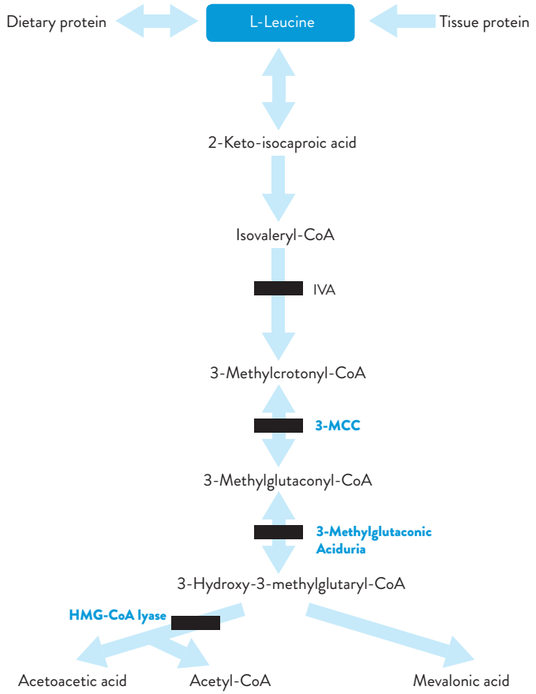
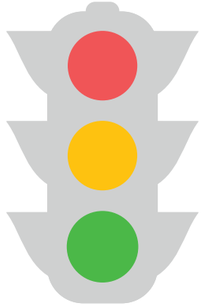


Figure 2. Metabolic pathway for LEU. The black boxes show the site of where there could be an enzyme that doesn't work, causing the noted disorders.

Think of the situation as a traffic light (Figure 3). A green traffic light (normal enzyme) allows LEU to be used normally. A red light (no or too little enzyme) keeps LEU from being used. If the light is stuck on red, a traffic jam occurs—LEU and organic acids increase in the blood and tissues and cause symptoms of a DLC.

If a person is not treated, LEU and organic acid also spill into the urine and perspiration (sweat).



Enzyme not working.
LEU cannot be broken down. LEU and organic acids build up in the blood and urine.

Enzyme not working well.
LYS and TRP may not be broken down efficiently.

GDH working.
LYS and TRP used normally. Breakdown products do not build up.

Figure 3. The disorders of leucine catabolism (DLC) traffic light.

DISORDERS OF LEUCINE CATABOLISM: AN INHERITED DISORDER

DLCs are genetic disorders inherited from both mother and father, just like other features such as eye and skin color. Genetic information, which determines each person's characteristics, is carried on pairs of genes in every cell in the body. These genes serve as blueprints, or patterns.

Each parent of a child with a DLC has one normal (●) and one altered DLC (●) gene. Each one of their offspring will have one gene from each parent and could have one of four gene sets (Figure 4).

A child who receives gene set A inherits two normal genes (● ●). Her body will make enough enzyme to use LEU normally. She will pass a normal gene on to each of her offspring.

A child who receives gene set B or C inherits one normal (●) and one DLC (●) gene. His body will make enough enzyme to use LEU normally, but he can pass on the DLC gene to his offspring. A person with this gene set—one normal and one DLC—is called a carrier. Being a carrier does not affect the person's health.

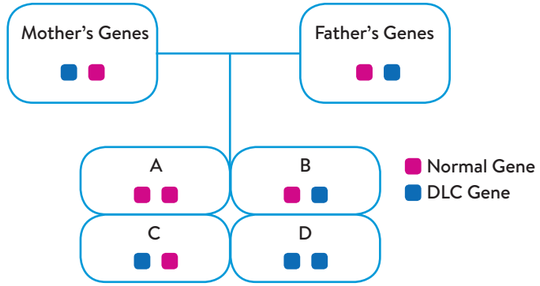


Figure 4. Genetic inheritance of DLC.

You, as parents of a child with DLC, are carriers. Brothers and sisters of your child with DLC may also be carriers.

A child with gene set D has DLC caused by the two DLC genes (● ●), one from the mother and one from the father. Her body will not be able to use the LEU in food normally. She will also pass a DLC gene on to each of her offspring. Your child with a DLC has this gene set.

TYPES OF DISORDERS OF LEUCINE CATABOLISM

There are four disorders of leucine catabolism considered to be branched-chain organic acidurias. The name of the deficiency generally refers to the enzyme affected. Dependent upon which disorder of leucine catabolism your child has will determine treatment methods. Your metabolic doctor and nutritionist will discuss which treatment method is best for your child.

Isovaleric Acidemia (I-so-val-air-ic a-cid-ee-mia), or IVA, is a deficiency of isovaleryl-CoA dehydrogenase (i-so-val-air-ill Co-A dee-hi-drog-en-ase) (IVD), that prevents LEU from being used in the body. Because LEU cannot be used normally, LEU or the products from its breakdown build up as isovaleric acid and other toxic (poisonous) substances. This excess keeps another important substance, coenzyme A (CoA), from working and causes the symptoms of IVA. A characteristic feature of IVA is a distinctive odor of sweaty feet. This odor is caused by the build-up of isovaleric acid in affected individuals. There are two different types of IVA—acute and chronic.

- **"Acute"** IVA infants appear normal at birth but develop poor feeding, vomiting, diarrhea, and drowsiness (lethargy) within first few weeks of life. A "sweaty-feet" odor of the blood and urine are noted. Some infants also exhibit severe acidosis seizures, high ammonia levels (hyperammonemia), low platelet count in the blood (thrombocytopenia), low number of white blood cells (neutropenia), low number of red and white blood cells and platelets (pancytopenia), and low calcium levels (hypocalcemia).
- **"Chronic Intermittent"** IVA children are normal at birth. During the first few years of life, they may develop episodes of vomiting, metabolic acidosis, and excessive tiredness (lethargy). The characteristic "sweaty-feet" odor is typically present, and temporary hair loss (transient alopecia) is usually seen. Episodes may begin as early as 2 weeks of age, and the frequency of attacks seems to decrease with age. Infections tend to trigger the episodes, as does illness and an excessive intake of protein.

Additional Therapies. The goal of nutrition management of IVA is to avoid too much isovaleric acid in the blood and urine while supplying energy, protein, vitamins, and minerals needed for normal growth and development. An LEU-free medical food with the addition of a low-protein diet (restricting LEU) is recommended. Your metabolic doctor may also recommend carnitine and/or glycine supplementation. Carnitine and glycine help the body get rid of toxic metabolites that build up in the body as well as help to prevent possible deficiencies.

3-Methylcrotonyl-CoA Carboxylase Deficiency (meth-ill-crot-o-nil Co-A car-box-ill-ase), or 3-MCC, is a deficiency in 3-methylcrotonyl CoA, blocking the body's ability to break down LEU (Figure 2). Children typically have normal growth and development until they have an acute episode between 6 months and 3 years of age. Symptoms have also been reported in the neonatal period and also as late as adulthood. Symptoms typically occur after an infection and may include poor muscle tone (hypotonia), or coordination, poor feeding, vomiting, excessive tiredness (lethargy), developmental delay, or symptoms resembling Reye's syndrome (low blood sugar [hypoglycemia], high ammonia levels in the blood [hyperammonemia], metabolic acidosis, elevated liver enzymes [transaminases], and seizures).

Additional Therapies. Nutrition management of 3-MCC deficiency involves management of the initial infection that triggered the 3-MCC symptoms, correction of carnitine deficiency (if present), and possible LEU restriction.

Nutrition management may include an LEU-free medical food paired with a low-protein diet (restricting LEU). Your metabolic doctor may also recommend carnitine and/or glycine supplementation. Carnitine and glycine help the body get rid of toxic metabolites that build up in the body as well as help to prevent possible deficiencies.

3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (3-hi-drox-ee 3-meth-ill-glue-tar-ill-Co-A lie-ase), also known as HMG-CoA lyase deficiency. This deficiency not only blocks the body's ability to break down LEU, but also prevents the body from making ketones (key-tones), which are used for energy during periods without food (fasting). HMG-CoA lyase deficiency symptoms may include vomiting, excessive tiredness (lethargy), metabolic acidosis, low blood sugar (hypoglycemia), high ammonia levels (hyperammonemia), and an enlarged liver (hepatomegaly), frequently triggered by an illness or fasting. Infection, high protein intake, and prolonged fasting can lead to metabolic decompensation, resulting in low blood sugar with a small amount or no ketones produced (hypoketotic hypoglycemia), and an increase in several organic acids. The inability to produce ketones in response to fasting can cause severe low blood sugar.

Additional Therapies. Paired with a low-protein diet (restricting LEU intake), additional therapies include prompt attention to illness, decreased fat intake, carnitine supplementation, and avoidance of fasting. The goal of long-term nutrition management is to prevent low blood sugar, limit long periods of fasting, and minimize elevations of LEU metabolites. A high-carbohydrate, low-fat diet with LEU restriction results in normal growth and development. A high carbohydrate intake with reduced fat intake is required to prevent the build-up of metabolites arising from the breakdown of stored body fat (fatty acid oxidation). Carnitine helps the body get rid of toxic metabolites that build up in the body as well as help to prevent possible deficiencies.

3-Methylglutaconic Aciduria Type I (meth-ill-glue-ta-con-ic a-cid-ur-ee-a) is a deficiency of methylglutaconyl-CoA hydratase (meth-ill-glue-ta-con-ill Co-A hi-dra-tase) that results from an increased amount of 3-methylglutaconic acid released and blocks the body's ability to break down LEU (Figure 2). Symptoms range from isolated speech retardation to slowing down of thought and a reduction in physical movement (psychomotor abnormalities), seizures, and nervous system impairment. Reye-like symptoms, including low blood sugar (hypoglycemia), acidosis, and high ammonia levels (hyperammonemia), have also been reported.

Additional Therapies. The goal of treatment during acute episodes is prevention of body protein breakdown (catabolism) by carbohydrate administration and correction of the acidosis. The effect of long-term nutrition management of this rare disorder has not been established. Nutrition management may include an LEU-free medical food paired with a low-protein diet (restricting LEU). Your metabolic doctor may also recommend carnitine supplementation. Carnitine helps the body get rid of toxic metabolites that build up in the body as well as help to prevent possible deficiencies.

DIAGNOSIS OF A DLC

Most states require all babies to be screened for disorders of LEU catabolism and other conditions before they are discharged from the hospital. In cases where DLCs are not tested on newborn screening, an individual may be diagnosed after showing symptoms of the condition.

If the initial screening tests show that a baby may have a DLC, additional blood and urine are collected for more precise measurements that will confirm the diagnosis. Some doctors may hospitalize the infant to confirm diagnosis so that treatment can be started sooner if the baby has a DLC.

NUTRITION SUPPORT OF A DLC

A diet that reduces LEU intake is used to help prevent most of the symptoms of a DLC. This diet, which is different for each person with a DLC, can lower the blood and urinary organic acid levels to a range that may allow normal mental development and growth.

The special diet for your child is designed for his individual needs, and following it is very important. With proper nutritional management, your child will grow and develop normally.

Many foods contain protein. Those foods also contain LEU. Your child with a DLC must limit the amount of foods that contain protein. Table 1 is a general guide of foods that are not allowed, foods that are limited, and foods that may be eaten freely if obesity is not a problem.

Table 1. General Guide to Foods on LEU-Restricted Diets

Foods That Are Not Allowed	Foods That Are Limited	Foods That May Be Eaten Freely
Dairy products (cheese, milk, ice cream, yogurt), soy milk and soy products, beans and peas, eggs, fish and seafood, meat, nuts, nut butters, poultry, seeds, tofu	Breast milk, infant formula, bread, crackers, fruit, fruit juices, low protein cereals, popcorn, potato chips, special low-protein foods, vegetables, vegetable juices	Gumdrop candy, hard candy, jelly, Kool-Aid®, lemonade, lollipops, Popsicles®, pure sugar and fat, soda

Requirements for LEU, Protein, and Energy. A child with a DLC who eats enough protein to grow properly gets too much LEU. Foods high in protein are cheese, milk, soy milk, eggs, meat, poultry, fish and seafood, nuts, beans and peas, seeds, and nut butters. Foods low in protein include some cereals, grains, fruits, fats, vegetables, and sweets. Eating these foods in the amounts needed to provide just enough LEU does not provide enough protein to meet your child's needs for growth. Depending on your child's protein tolerance, a special medical food that is high in protein and free of LEU may be required..

To be sure your child is getting enough energy, protein, and adequate LEU for growth and development, a nutritionist carefully calculates the amount of each nutrient needed. Too little LEU, protein, or energy can result in growth failure. Frequent diet adjustments are necessary, especially during the first 6 months of life when babies grow rapidly. The nutritionist or metabolic doctor will make these diet changes based on your baby's health, growth, LEU intakes, blood levels of LEU, and urinary excretion of organic acids.

I-Valex®-1 Amino Acid-Modified Medical Food With Iron is a medical food used to provide protein for infants and toddlers. I-Valex-1 does not contain any LEU. Similac Advance Infant Formula with Iron, breast milk, or other intact protein must also be fed to provide the specific amount of LEU your baby needs for growth and development. Breast milk is lower in LEU than infant formula or cow's milk and can be used to supply the required LEU. The decision to breastfeed should be discussed with your nutritionist and metabolic doctor. The nutritionist or metabolic doctor will tell you the exact amount of breast milk needed in addition to your child's medical food. I-Valex-1 contains carnitine and is well supplied with fat, carbohydrate, minerals, and vitamins. Supplemental minerals and vitamins are not usually needed when the diet is followed as directed.

I-Valex®-2 Amino Acid-Modified Medical Food With Iron is a medical food used for treating children and adults with a DLC. I-Valex-2 contains no LEU, so LEU must be met by using other food sources. Your nutritionist will tell you which medical food is right for your child, as well as which foods and how much of each your child can eat. I-Valex-1 and I-Valex-2 must be used under the supervision of a physician.

I- Valex-1 and I-Valex-2 taste different from milk. Most children and adults get accustomed to the flavors of the foods that they eat. They may seem distasteful to you, but it is very important not to show this to your child, either by word or action. Your child may refuse the medical food just because you appear not to like it.

One mother disliked the odor of the medical food so much that she made a face every time she gave it to her son. Because of this, he refused the medical food for several days until she and her family realized what was wrong. As she said later, "We changed our attitude to thinking this wonderful diet will make it possible for our child to have a happy life."

Other children in the family should be told that I-Valex is very important, and they should not emphasize the difference in taste or odor between milk and medical food to the child with a DLC.

Most children taking medical foods for a DLC like them IF the medical foods are started early and IF their family has a positive attitude. Older children who start on the diet after drinking cow's milk may not like I-Valex at first, but in time accept it.

Table 2. Metric to English Conversions

Metric		English
Solids		
1 g (0.001 kg)	=	0.035 oz
28 g	=	1 oz
454 g	=	1 lb
1000 g (1 kg)	=	2.2 lb
Liquids		
5 mL	=	1 tsp
15 mL	=	1 Tbsp
60 mL	=	1/4 cup
240 mL	=	1 cup
1000 mL (1 L)	=	4 1/4 cup (1.06 qt)

Flavorings, such as Kool-Aid® Unsweetened Soft Drink Mixes, Wyler's® Unsweetened Soft Drink Mixes, and concentrated fruit juices can be added to I-Valex. I-Valex may be made into a paste and combined with some allowed fruits, such as applesauce or other fruit purees, or combined with instant pudding mixes. Check the label, and be careful which pudding mixes you buy, as some contain more protein than others.

INTERNATIONAL SYSTEM OF MEASUREMENT (METRIC SYSTEM)

The metric system is the International System of Measurement. It is used for all medical and scientific measures.

In the metric system, solids are weighed in grams (g) or kilograms (kg) and liquids are measured in milliliters (mL) or liters (L). A list of common conversions from the metric system to the English system used in the United States is given in Table 2. The most accurate method to be sure your child is getting the proper amount of LEU is to weigh foods on a scale that reads in grams.

Medical Food Preparation. Mix a 24-hour supply of medical food at one time or as instructed by your nutritionist.

Tips for preparing formula for infants:

- **Always follow the instructions on the label and mix formula according to the recipe provided by your nutritionist or metabolic doctor.**
- Wash your hands and all supplies carefully before preparing formula.
- Do not mix longer than indicated on the I-Valex label.
- Always test the temperature of heated formula before feeding by shaking a few drops on your wrist.
- Overmixing causes the fat emulsion to break. Separation of the medical food mixture then occurs. Overmixing may also add air that destroys vitamins A and C.
- Heating above 100° F (37.8° C) or adding hot water may cause loss of vitamins A and C and lead to the Maillard reaction—a reaction in which some amino acids bind with carbohydrate, making them unavailable to the child.
- Mix in the approved natural protein (breast milk or infant formula) if recommended by your nutritionist or metabolic doctor.
- Refrigerate the medical food after mixing. Discard any unused medical food 24 hours after mixing because of nutrient loss.

Feeding Your Infant. The way you feed your baby with a DLC is the same as for any baby. The I-Valex-1 formula will be supplemented with breast milk or infant formula such as Similac Advance EarlyShield. The nutritionist may have you mix the two

Feeding time should be a pleasant experience for you and your baby.

formulas together. The I-Valex-1 mixture stored in bottles in the refrigerator may be warmed before feeding.

- Shake the formula mixture and pour into a bottle.
- Set a bottle in a pan of cold water on the stove and gradually warm it or run hot tap water over the bottle.
- Never use a microwave oven to warm formula as this can result in hot spots that can burn your baby.
- Always test the temperature of heated formula before feeding by shaking a few drops on your wrist. The formula should feel lukewarm.
- If the I-Valex-1 mixture drips freely, the nipple holes are the correct size. Shake the bottle well before feeding.

To feed your baby, sit in a comfortable place, hold her in the curve of your arm, and keep the nipple filled with the I-Valex-1 mixture so that air will not be swallowed. You should burp your baby at least once during and again at the end of each feeding. Hold her upright against your shoulder or lay her face down on your lap and gently pat her back.

DO NOT WARM THE BOTTLE IN THE MICROWAVE.
Uneven warming may cause serious burns.

Introduction of Solid Foods. No baby is born with the ability to swallow solid foods. The swallowing reflex develops at 2 to 3 months of age. Before this time, the baby's "tongue thrust" causes the tongue to protrude, making swallowing food difficult. Waiting to feed solid foods until the baby is developmentally ready is best.

I-Valex-1 is similar to infant formula, and the amounts, as well as the kinds of cereals, fruits, and vegetables prescribed are about the same as would be fed any baby. Your baby's nutritionist or metabolic doctor will advise you about when your baby should start eating infant cereal and strained baby foods, and which foods to introduce. Guidelines for adding various foods to your baby's diet are given in Figure 5. However, your nutritionist or metabolic doctor may suggest different ages. Follow their advice.

At about 7 to 8 months of age, your child may begin trying to eat foods such as crackers, low-protein toast, or pieces of fruit without help. At about 9 months of age, your child may begin using a spoon.

If your 9- to 12-month-old child has never eaten without help, dip her fingers into the food to give her the idea of finger feeding. Later, you can teach her to pick up a spoon and help guide it to her mouth. Putting your child on your lap to guide her hand may be easier. Start with thick foods such as mashed potatoes since they do not slip off the spoon easily.

Do not worry if your child does not eat all of the foods you measure out; just estimate what was not eaten, replace the LEU with another food, and write it down.

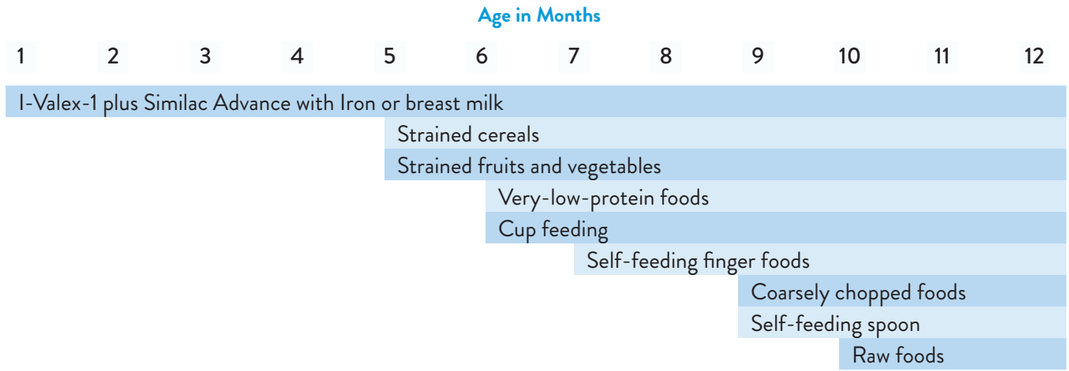


Figure 5. Suggested timetable for beginning solid foods and self-feeding.

When your child is older, the differences between the LEU-restricted diet and the diets of other children will be greater. Your child with a DLC will require I-Valex all her life to provide most of her protein, mineral, and vitamin needs.

Diet Guide and Food Lists. At each clinic visit, you will be given guidance that spells out in detail what your child can eat. The amount and how to prepare the medical food mixture, as well as the types and amounts of food that your child is allowed, will be outlined. The nutritionist will help you work out a plan that meets your child's needs and fits into the family budget and lifestyle.

Lists of foods make meal planning easier and help you be sure your child's nutrient needs are met. You will have time to become familiar with the food lists and their nutrient content, because foods will be added slowly to your child's diet.

When your child is older, you may need to use Free Foods (see Table 1) to meet her energy needs. Free foods, which are high in energy and contain little or no LEU, must not replace prescribed foods nor be used in large amounts. If your child eats too many of these free foods, she may become overweight, or the extra sugar may cause tooth decay. Special low-protein foods, including pasta, rice, crackers, cookies, and breads, can be added to the diet. These foods will help satisfy your child's hunger.

If you are not able to find the LEU content of a certain food, ask your nutritionist. The nutritionist can calculate the nutrient composition of the food and help you include it in the diet plan if it is not too high in LEU.

Be sure to check with the nutritionist before using any food that is not on the food lists provided.

CHECKING YOUR CHILD'S PROGRESS

Laboratory Tests. Because your baby grows rapidly during the first year of life, blood and urine samples will be tested frequently to monitor how well her DLC is controlled, and to indicate if changes in treatment are needed. Your doctor may ask for a blood and/or urine sample once or twice a week during your baby's first 6 months, then once every 2 weeks until 1 year of age. After 1 year of age, checking blood and urine levels and diet records may be decreased to once a month if blood LEU and organic acid levels are well controlled. Various methods are used to monitor the amino acids and organic acid levels in the blood and urine. Your baby's metabolic doctor or nutritionist will determine how often your child is tested.

Before taking a blood sample, you may be asked to accurately record your child's total food and beverage intake. In this food diary (notebook or form the clinic may provide), record the name of the food, the exact amount in grams or household measures (cups, teaspoons, or tablespoons) that your child ate, and the LEU content based on the food lists or information given to you by the nutritionist. This will help the metabolic doctor and nutritionist evaluate your child's laboratory test results.

Urine Tests. A urine test may be requested by your metabolic doctor to monitor metabolic control. When a child is not getting enough calories, his body fat and protein may be used for energy. In certain DLCs (ie, HMG-CoA lyase deficiency), breakdown of body fat and protein may release ketones and organic acids, which can affect his health. Ketones may be detected in the urine by the use of Ketostix®. Daily testing of the first urine in the morning will provide information useful in managing your child's diet.

LEU and Organic Acid Levels. The amount of LEU in the blood is an indirect measure of how much LEU is present in body tissues. Of most concern is the brain, because too much LEU, organic acid, and ammonia, as well as too little sugar, are harmful to brain development. Because blood transports nutrients to the brain, the concentration of LEU, organic acid, and sugar in the blood will give the doctor and nutritionist an idea of how much of these substances might be in the brain.

Blood LEU levels that are high may indicate that your child is eating more foods that are high in LEU than his body needs for growth. Illness, such as colds and flu, can also cause the body to break down its own protein, releasing LEU into the blood. When your child is not getting enough protein, because of rapid growth or inadequate intake of the medical food, the blood LEU levels may also rise. Initially during rapid growth, the blood LEU level will decrease and then increase again as the body breaks down its own protein.

A low LEU level usually indicates that your child is not getting enough LEU in the diet.

Clinic Visits. Because a DLC is a lifelong condition that could harm your child's growth and development, you will be asked to take your child to the clinic frequently. If growth and development are normal and laboratory concentrations remain within treatment range, the frequency of clinic visits may be decreased with time.

At clinic visits, your child may be given developmental, physical, and neurological tests. Family interaction, which is important to your child's development, may also be evaluated. Diet changes will be made, if needed, and any questions you may have will be addressed.

In addition to the metabolic specialist, you should have a local pediatrician or family doctor to provide required ongoing well-child care. This doctor should give immunizations at the usual times, or you may obtain them from the health department.

YOUR CHILD'S GROWTH AND DEVELOPMENT

By 4 to 6 months of age, your infant's birth weight will double. The child with a DLC whose LEU intakes are well controlled and whose diet supplies adequate nutrients should grow as well as a child without a DLC.

During the second 6 months of life, the growth rate decreases. Your child may grow 1 inch (~2.5 centimeters [cm]) per month during the first 6 months and 4 inches (~10 cm) total during the second 6 months of life. This normal decline in the growth rate usually causes a decrease in appetite.

Although the requirement for energy (calories) and protein based on body weight decreases, the total daily requirement for most nutrients increases with age. You will need to adjust food choices accordingly to ensure that your child has an adequate nutrient intake. The nutritionist will help you with food selections that are right for your child.

Weaning from Bottle to Cup. When the time comes to switch from the bottle, your child may need extra attention, as any child would. Weaning takes patience, especially if your child shows no interest in drinking from a cup or a glass.

Begin offering I-Valex-1 from a cup when your child is between 5 and 8 months of age. Because taste buds vary on different parts of the tongue, I-Valex may taste different when taken from a cup instead of a bottle. Also, the smell of I-Valex

may be more pronounced in an open cup. Some parents find a training cup that has a lid and a spout to be very useful. Offering the I-Valex at a cold temperature may also increase your child's willingness to drink from a cup.

During weaning, your child may not want to take all the prescribed I-Valex in liquid form. You may offer some of it in instant puddings, cereals, fruits, and soups, or it can be mixed into a paste with fruits and fed by spoon.

ADDITIONAL WATER MUST BE OFFERED WHEN I-VALEX® IS FED AS A PASTE. Consult your child's nutritionist.

A child of 15 to 18 months of age may drink more medical food from a cup if she is given a small pitcher of I-Valex and is encouraged to pour it into a small cup without help. Many parents have found using brightly colored straws, special cups, or sports bottles to be good transitional tools to help wean a child from the bottle.

Toddlers. Toddlers, children from 1 to 3 years of age, have a slow growth rate compared with that of infants. Toddlers may gain 4 to 5 pounds (1.8–2.3 kilograms [kg]) a year, compared with the infants' gain of 12 to 22 pounds (5.5–10 kg) per year.

Growth during this period involves changes in body form. Legs lengthen and body fat decreases. Energy needs are decreased because of the slower growth rate. However, mineral and vitamin needs increase.

Toddlers seek independence and are very curious about their environment. Because toddlers want to do things for themselves, encourage your child to feed himself.

Preschoolers. Preschoolers also have a slow weight gain of 4 to 5 pounds (1.8–2.3 kg) per year. On the other hand, their total energy needs are greater than those of toddlers. Because your preschooler's nutrient and energy needs are greater, the nutritionist may tell you to increase foods with a high nutrient content. These foods are packed with vitamins and minerals and are energy dense.

Let your preschooler make some decisions. For example, permit him to choose which cereal, fruit, or vegetable to eat. Be aware that most preschoolers want to do things at their own speed. Be prepared to have your child spend so much time talking that little is eaten. This is normal behavior.

Social Interaction at Mealtime. Mealtime is an important part of every child's social development and, whenever possible, the family should eat together. Younger children can learn how to feed themselves by watching older brothers and sisters.

Make meals for your child with a DLC as similar as possible to the family's meals. Menus for him can be planned from those for the rest of the family. For example, whenever possible, use the same fruits and vegetables for everyone. You can also prepare a low-protein pasta or meatless dish that is similar to the one served to other family members. The family's help and support are very important to maintaining the diet.

TEACHING YOUR CHILD DIET MANAGEMENT

Explaining the diet can begin by calling allowed foods "special" or "just for you." From the time your child is very young, teach her to ask about unfamiliar foods before eating them. As your child grows older and is able to understand the concept of a missing or nonworking enzyme, explain the DLC. Some materials that you may find helpful are listed on page 15.

Toddlers and Preschoolers. Permit your preschooler to make food choices, such as what fruit he wants to eat. Plan meals that have variety in color, texture, flavor, and preparation methods. A child who is involved in food selection and preparation will be more interested in trying a new food. Involve your child in planning menus to become familiar with foods allowed and excluded. Let him help grocery shop, set the table, and prepare the food.

At about 3 to 4 years of age, children want to serve themselves. Teach your child the proper food portions. One way to do this is to use a "token" system. Tokens symbolizing 5, 15, or 30 mg of LEU, or 1 gram of protein, may be used to "purchase" foods containing these amounts.

School Age. When your child reaches school age, she will become more independent in many aspects of her life and eating is one of them. As she begins to develop logic and math skills, it is important she use these skills to understand the diet. Encourage your child to help prepare the medical food and calculate the amount of LEU in foods. As your child gets older, she should understand what levels of LEU are considered normal and the consequences of high LEU levels.

Adolescence. Adolescence may be a difficult time for both you and your child, regardless of the DLC! The influence of friends and the struggle for independence may make dietary compliance a challenge. Teens may feel that the DLC makes them different from their friends. Eating out with friends is part of growing up. Help your child develop the skills for eating out, traveling, and "sticking" to the diet when not at home. Sometimes teenagers with a DLC would rather tell people they are vegetarian or vegan than explain about the DLC. Help your teenager deal with her peers and not be self-conscious that she has a DLC. Finding a peer with a DLC through support groups can be a great comfort for a teen. Ask the clinic for resources and suggestions.

FEEDING PROBLEMS

Parents may be tempted to treat their child as a "sick" child and not follow their usual patterns of child rearing. The child with a DLC is a normal child who needs to manage food intake carefully. Ask your child's doctor, nutritionist, public health nurse, or social worker for support and help if any of the following problems should occur.

Loss of Appetite. Loss of appetite can result from a variety of causes including poor metabolic control; illness; eating too many sweet foods or desserts that satisfy the appetite and decrease the desire to eat the foods prescribed; getting too much I-Valex, which may depress the appetite for other foods; or having a lower than normal blood LEU level. Medications may also decrease appetite.

Unusual Hunger. This may be an indication that the diet needs to be adjusted. The amount of I-Valex may need to be increased because the table foods prescribed are not satisfying needs. Using low-protein foods is a great way to manage hunger without increasing protein intake.

Refusing Medical Food. A child may refuse I-Valex because of normal variations in appetite, and this should not be of concern if average intake over a week is adequate. If I-Valex is not offered regularly, a child may decide to refuse it. Improperly mixed I-Valex also can cause refusal— too much water makes the volume too great; too little water makes the I-Valex mixture too thick. A child may refuse I-Valex as an attention-getting device, especially if he senses that his parents are anxious for him to drink the I-Valex mixture. Remember, I-Valex plays an important role in providing most of your child's nutrition needs. If refusal of the medical food continues to be a problem, the use of a feeding tube may need to be considered.

Refusing Solids. A child may experience normal variations in appetite or taste for certain foods. The prescribed amount of I-Valex may be too high and the energy in it is causing her to lose her appetite.

Toddlers and preschoolers periodically have one of two characteristic feeding behaviors that cause parents concern. They may decide to stop eating by going on a "food strike," or they may go on a "food jag." Food jags and strikes are common among young children.

During a food strike when your child refuses to eat, offer food at usual mealtimes, and if she refuses the food, take it away. Allow only water between meals. She will become hungry and then eat. **Remember that I-Valex supplies most of your child's nutrient needs, so her medical food should never be restricted.**

Do not give in to a food strike and offer Free Foods or foods that are not on the LEU-restricted diet. The nutritionist can help you during this trying time, so do not hesitate to call. It is also very important for both parents to support each other in managing a food strike. If a child is allowed to eat foods not on her diet, LEU levels will not be controlled.

On a food jag, a child wants to eat the same food or foods for long periods. If the foods are nutritious and are in the diet, there is no reason for concern. Remember that most of your child's nutrient needs are supplied by I-Valex.

Inappropriate Feeding Behavior. Inappropriate feeding behaviors, such as refusing to give up the bottle and/or difficulty in eating solids, chewing, or self-feeding, may result from a variety of causes. These can include a delay in offering table foods, delay in teaching the child to drink I-Valex by cup, or not allowing the child to feed himself either with fingers or spoon. Always keep a positive attitude and make feeding a pleasurable event.

Try not to feed a child longer than necessary at mealtime to encourage self-feeding. Remember that small amounts of food are usually wasted when a child first learns to self-feed, but this is normal. Keeping food records will help your nutritionist estimate your child's intake.

A child may be using his diet as a way of getting attention or manipulating parents. If your child has any of these problems, call the nutritionist. The nutritionist will give you support and offer suggestions to help solve the problem.

THE ROLE OF FAMILY AND OTHER CARE PROVIDERS IN MANAGING A DLC

Parents carry the bulk of the responsibility for managing their child's DLC. If possible, try to share the responsibility in preparing meals and monitoring your child's diet. Other children in the family, as well as the child with a DLC, should learn about the diet as soon as they are old enough to understand it. Older brothers and sisters should be encouraged to be involved in feeding the child with the DLC so they become familiar with foods allowed and excluded. Make sure they understand the importance of the diet for their brother's or sister's health. Brothers and sisters should not feel sorry for the child with the DLC because he is on a special diet. Treat your child with a DLC as normally as possible.

Grandparents love to spoil their grandchildren! It may be difficult for them as they sometimes feel the child with the DLC is "missing out." It is important they understand the

diet and become actively involved as much as possible. A grandmother may be the ideal person to experiment with low-protein cooking and provide special low-protein treats.

Explain the DLC to relatives, friends, day-care providers, baby-sitters, and all teachers. They should become familiar with foods allowed and excluded, and understand the importance of the diet. Give a list of the foods allowed and not allowed to anyone who feeds your child and explain the list as well as the exact menu.

Tell everyone who cares for your child that even "just a little bite" of a high-protein food is not allowed. Emphasize what can happen if your child does not stay on the diet.

YOUR CHILD'S DIET DURING ILLNESS

A body temperature greater than 98.6° F (37° C) or a rectal temperature over 100° F (37.8° C) is a fever. During fever, the body's rate of using food for energy speeds up. If extra energy is not supplied during illness, the body will break down its own muscle protein and fat stores for energy. Muscle protein breakdown (and fat breakdown in some DLCs) needs to be prevented in children with a DLC because it will release too much LEU and organic acids into the blood. LEU and organic acids are carried to the brain and other body organs where they may have a harmful effect. Give your child extra low-protein food, formula, and fluids during illness. The extra food will decrease the amount of muscle protein broken down for body energy.

Feeding an ill child can be very difficult. Often a child with fever is restless and has a loss of appetite. The illness might also include stomach upset, nausea, or vomiting. A child may become very dehydrated because of the high body temperature and a lack of adequate fluid intake.

If you suspect a cold or virus, or if your child has a fever, it is important to call your pediatrician or metabolic doctor immediately. Illness in a child with a DLC can be very serious. Your metabolic doctor or nutritionist will help you decide on how to manage it.

Ask your nutritionist for a "sick-day plan" to use during illness. A sick-day plan provides adequate calories to meet energy needs and helps keep your child out of the hospital. Ask about using medication such as acetaminophen (Tylenol®) to reduce fever.

Here are some suggestions of things to do when your child is ill with fever.

- Do not force-feed food or I-Valex, especially if your child is nauseated or vomiting. Soda crackers may be the only food he will feel like eating. Encourage intake of any allowed foods that your child is willing to eat.
- Encourage your child to continue drinking his medical food if he tolerates it.
- Offer Pedialyte® Oral Electrolyte Solution with added carbohydrate, such as dextrose or table sugar (3 Tbsp sugar to 8 fl oz of Pedialyte); Pro-Phree®; non-cola carbonated beverages; sugarsweetened carbonated beverages; Kool-Aid®; Tang®; tea with sugar; vegetable broth; or fruit juices with some sugar added.
- Dilute the I-Valex mixture, or use liquid Jell-O® if it is tolerated.
- Freeze any of the beverages listed and make into chipped ice. Frequently feed small amounts of this chipped ice to provide energy and prevent dehydration.
- As your child's appetite improves, gradually return to the usual diet plan.

Emergency Letter. Individuals with DLC should have an emergency letter with them at all times. This letter provides important information such as the name of the condition, explanation of symptoms, the importance of timely treatment and treatment strategies, and your metabolic doctor's contact information. In times of illness or stress that may require hospitalization, this letter can be presented. This letter can be provided by your metabolic team.

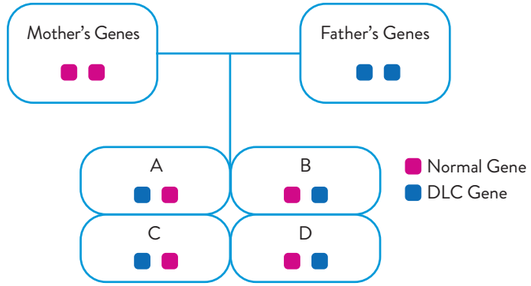


Figure 6. All children of a person with a DLC and a person who does not have a DLC will be carriers of a DLC.

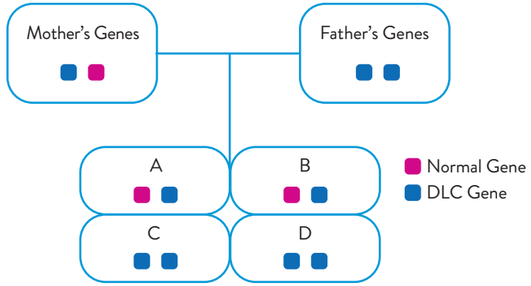


Figure 7. Approximately half of the children of a parent with a DLC and a parent who is a carrier of a DLC will have a DLC.

A LOOK TO THE FUTURE

Continuing the Diet. A DLC is a serious health concern. Treating a child as early in life as possible may prevent developmental delay and severe neurological damage. Not following the LEUrestricted diet may cause mental and neurological damage at any age. Lifelong nutrition support must be adapted to each person's needs. Metabolic doctors and nutritionists provide support that is essential for helping your child have a normal, productive life.

Family Planning. The chance that two carriers of a DLC will have a child with a DLC is 1 in 4, or 25%, for each pregnancy (Figure 4). Because you have a child with a DLC, you know that both parents are carriers. That means you have a 25% risk with each pregnancy of having another child with a DLC. The chance that two carriers will have a child who is a carrier is 1 of 2, or 50% for each pregnancy.

Before a couple with a child who has a DLC plan to have any more children, they should take time to seriously think about the special parenting tasks that parents of a child with a DLC must manage. Genetic counseling is recommended to review the risks, and to discuss several reproductive options that are available before and during pregnancy.

While there is no test that can determine if another child will be affected with a DLC before a pregnancy, prenatal testing may be possible during the early part of the pregnancy. A couple may want to discuss and consider all their options with their metabolic doctor and genetic counselor before another pregnancy.

If you decide to have another child, give yourselves time to adjust to providing for the special needs of the first child. Parents will want to be skilled in diet management for the DLC before having another child.

Offspring of a Person with a DLC. All children born to a person with a DLC will be carriers of the gene or have a DLC. As shown in Figure 6, all offspring of a parent with a DLC ( ) and a parent who is normal( ) inherit one normal ( ) and one DLC ( ) gene. Each one of their children will be a carrier. If a person with a DLC has children with a carrier for DLC, approximately onehalf (50%) of their offspring will have a DLC and one-half (50%) will be carriers (Figure 7).

Childbearing by Women with a DLC. For the woman with a DLC, having children may cause problems. A major concern for the DLC women is the stress of the pregnancy on her metabolic control. The nutritional requirements can rapidly change during the course of a pregnancy. Pregnant women must be monitored carefully for their own safety, as well as the health of their baby.

DLCs are a serious health concern. However, by following an LEU-restricted diet closely and keeping blood LEU levels within the treatment range, the person with a DLC can lead a normal, productive life. Successful pregnancies require attentive diet monitoring during the prenatal, labor, delivery, and postpartum periods.

Kool-Aid®-Flavored I-Valex®-1

Yield: 8 fl oz

40 g I-Vales-1
3 Tbsp, **level**, sugar[1]
1/4 tsp Kool-Aid or Wyler's® **Unsweetened** Soft Drink Mix

Add water (room temperature) to ingredients to make 8 fl oz. Mix in a blender at lowest speed no more than 4 seconds. Or, shake briskly in a closed container for 10 to 12 seconds. Serve chilled.

Nutrient	*1 fl oz*	*8 fl oz*
Lysine, mg	0	0
Protein, g	0.75	6
Energy, kcal	42	336

[1] Osmolality (concentration of particles in solution) may be too high if more sugar is added, which may cause bloating and diarrhea.
[2] The amount of drink mix may be varied according to taste preference.

Fruit Juice-Flavored I-Valex®-2

Yield: 8 fl oz

20 g I-Valex-2
3 fl oz concentrated apple, grape, or orange juice
Water (room temperature) to make 8 fl oz

Warm juice concentrate to room temperature. Place all ingredients in a blender at lowest speed no more than 4 seconds. Or, shake briskly in a closed container for 10 to 12 seconds. Serve chilled.

Nutrient	*Apple juice*	*Grape juice*	*Orange juice*
Lysine, mg	33	15	48
Protein, g	6.5	6.7	8.6
Energy, kcal	257	275	252

[1]Please check with your dietitian or doctor before using this recipe in infants.

Kool-Aid®-Flavored I-Valex®-2

Yield: 16 fl oz

40 g I-Valex-2
3 Tbsp, level, sugar[1]
1/2 tsp Kool-Aid or Wyler's **Unsweetened** Soft Drink Mix[2]

Add water (room temperature) to ingredients to make 16 fl oz. Mix in a blender at lowest speed no more than 4 seconds. Or, shake briskly in a closed container for 10 to 12 seconds. Serve chilled.

Nutrient	*16 fl oz*
Lysine, mg	0
Protein, g	12
Energy, kcal	308

[1] Osmolality (concentration of particles in solution) may be too high if more sugar is added, which may cause bloating and diarrhea.
[2] The amount of drink mix may be varied according to taste preference.

Additional Tips for Flavoring I-Valex Medical Food

- Add chocolate or strawberry syrup.
- Mix I-Valex with fruit to make a "smoothie."
- Freeze flavored medical food into "slushies" or "popsicles."
- Add dry I-Valex to pudding (lemon, tapioca, vanilla, etc) mixture. Prepare pudding with non-dairy creamer.

Use low-protein food lists to calculate LEU content of flavorings.

Support Groups/Newsletters

Organic Acidemia Association
Kathy Stagni, Executive Director
9040 Duluth St.
Golden Valley, MN 55427
Email: mkstagni@gmail.com
Phone: (763) 559-1797 (Central Time)
Fax: (866) 539-4060 (Toll Free)

Menta Pitre, Director
201 E. 14th Place
Larose, LA 70373
E-mail: menta@ooanews.org
Phone: (985) 856-5631 (Central Time)

Low-Protein Food Suppliers

Canbrands Specialty Foods, Inc.
3500 Laird Rd.
Mississauga, Ontario, Canada L5L 5Y4
Phone: (905) 829-6003
Email: helpdesk@canbrands.ca
Web site: www.canbrands.ca

Dietary Specialties
8 S. Commons Rd.
Waterbury, CT 06704
Phone: (888) 640-2800
Web site: www.dietspec.com

Ener-G® Foods, Inc.
5960 First Avenue South
Seattle, WA 98108
Phone: (800) 331-5222; (206) 767-3928
Fax: (206) 764-3398
E-mail: customerservice@ener-g.com
Web site: www.ener-g.com

Med-Diet™ Laboratories, Inc.
3600 Holly Lane, Suite 80
Plymouth, MN 55447
Phone: (800) 633-3438 (MED-DIET);
(763) 550-2020
Fax: (763) 550-2022
E-mail: info@med-diet.com
Web site: www.med-diet.com

PKU Perspectives
PO Box 696
Pleasant Grove, UT 84062
Phone: (866) PKU-FOOD; (801) 785-7722
Fax: (866) 701-3788
Web site: www.pkuperspectives.com

Taste Connections, LLC
Phone/Fax: (310) 371-8861
E-mail: tasteconnect@verizon.net
Web site: www.tasteconnections.com

IMPORTANT PHONE NUMBERS

Nutritionist: _____

Metabolic Doctor: _____

Pediatrician: _____

Police: _____

Fire: _____

Hospital: _____

Other: _____

_____

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We Help determine available coverage options

STEP 3
We Connect your covered patients to a supplier

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Maple Syrup Urine Disease

Urea Cycle Disorders

Propionic and Methylmalonic Acidemia

Glutaric Aciduria Type I

Tyrosinemia

Isovaleric Acidemia and Disorders of Leucine Metabolism

Homocystinuria

Dietary Modification of Protein

Hypercalcemia

Ketogenic Diet Management Carbohydrate Disorders

Dietary Modification of Carbohydrate and Fat

Use under medical supervision.

Abbott Metabolic Medical Foods

I-Valex® is part of an extensive line of medical foods from Abbott, makers of Similac®

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