Abbott

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

Methylmalonic Acidemia

CONTENTS

Abbott provides this booklet to health care professionals to help them counsel families, and to families to help them learn about MMA.

INTRODUCTION TO METHYLMALONIC ACIDEMIA

Your child has a condition called methylmalonic acidemia (meth-il-ma-lon-ic a-cid-em-i-a) or MMA for short. Children who have inherited this condition cannot use the amino acids *isoleucine* (i-so-lu-seen) (ILE), *methionine* (me-thi-o-neen) (MET), *threonine* (three-o-neen) (THR), *valine* (vay-leen) (VAL), and some fats in a normal way.

These amino acids are 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 amounts of ILE, MET, THR, VAL, and specific fats 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.

WHAT IS MMA?

MMA is an inherited disorder of amino acid and odd-chain fatty 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. Nine of these amino acids are called "essential amino acids" because the body must have them to live, and the only way to obtain them is through the diet. Four of these amino acids are ILE, MET, THR, and VAL.

All foods with protein contain ILE, MET, THR, and VAL. 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 ILE, MET, THR, and VAL. 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).

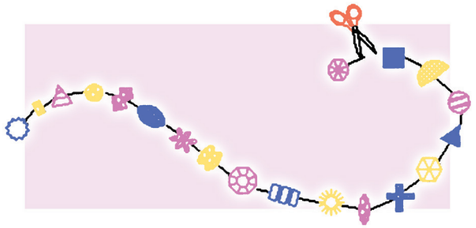


Figure 1. Amino acids are joined together like beads on a necklace to form protein. Enzymes act like scissors to remove amino acids from protein.

Once ILE, MET, THR, and VAL are split off from food protein, they are absorbed, changed, and used to form many other useful substances in the body.

Excess amounts of these amino acids and some fats are broken down by the enzyme called methylmalonyl CoA mutase (meth-il-malo-nil Co-A mu-tace), or MCM, to produce energy. In addition, vitamin B12 must be present in adequate amounts and in the proper form, called adenosylcobalamin (ad-ee-no-sil-co-ball-a-min), for MCM to work. MMA happens when either the MCM enzyme or an enzyme that helps to provide adenosylcobalamin is absent or not working normally. People with MMA, such as your child, either do not have enough normally working MCM or enough adenosylcobalamin. In either case, ILE, MET, THR, VAL, and some fats that are in the foods they eat cannot be used normally. They are changed and build up in the body as the organic acids methylmalonic acid and propionic (propee-on-ic) acid, which are toxic (poisonous) to the body when present in too large an amount. This build-up of organic acids keeps another important substance, coenzyme A (CoA), from working. All of this together causes the symptoms of MMA.

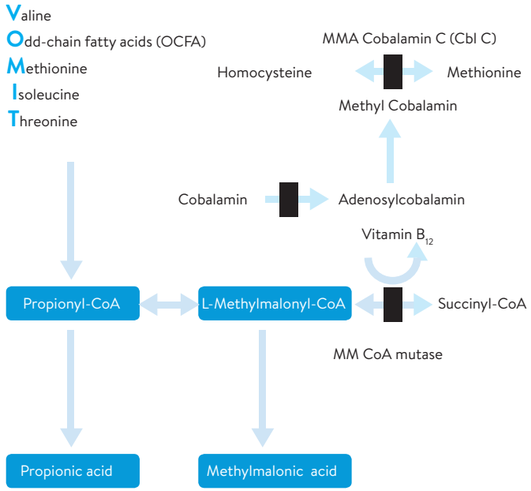
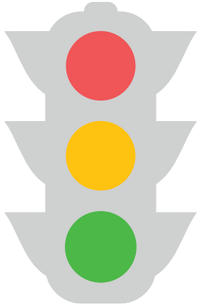


Figure 2. Metabolic pathway for ILE, MET, THR, VAL, and some fats in MMA. Substances in the shaded boxes are organic acids that build up when MCM does not work.

Think of the situation as a traffic light (see Figure 3). A green light (normal MCM) allows ILE, MET, THR, VAL, and odd-chain fatty acids to be used normally. A red light (no or too little MCM) keeps ILE, MET, THR, VAL, and some fats from being used. If the light is stuck on red, a traffic jam occurs and the ILE, MET, THR, VAL, oddchain fats, and toxic organic acids they create increase and cause the symptoms of MMA. If a person is not treated, these products build up in the blood and spill into the urine and sweat.



MCM not working.
ILE, MET, THR, VAL, and certain fats cannot be broken down. Organic acids build up.

MCM not working well.
ILE, MET, THR, VAL, and certain fats may not be broken down efficiently.

MCM working.
ILE, MET, THR, VAL, and certain fats used normally. Breakdown products do not build up.

Figure 3. The methylmalonyl CoA mutase (MCM) traffic light.

MMA: AN INHERITED DISORDER

MMA is a genetic disorder 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 for making body tissues and enzymes such as MCM.

Each parent of a child with MMA has one normal (●) and onealtered (MMA) (●) 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 MCM to use ILE, MET, THR, VAL, and odd-chain fatty acids 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 MMA (●) gene. His body will make enough MCM to use ILE, MET, THR, VAL, and odd-chain fatty acids normally, but can pass on the MMA gene to his offspring. A person

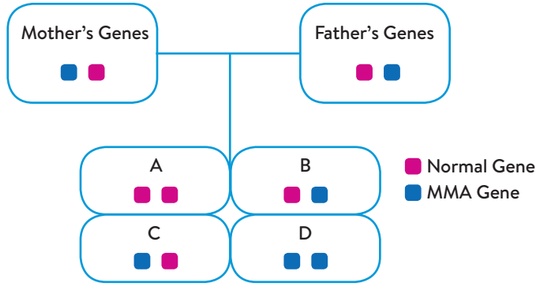


Figure 4. Genetic inheritance of MMA.

with this gene set —one normal and one MMA—is called a carrier. Being a carrier doesn't affect the person's health. **You, as parents of a child with MMA, are carriers.** Brothers and sisters of your child with MMA may be carriers, too.

A child with gene set D has MMA caused by the two MMA genes (●●) , one from her mother and one from her father. Her body will not be able to use the ILE, MET, THR, VAL, and odd-chain fatty acids in food normally. She will also pass an MMA gene on to each of her offspring. Your child with MMA has this gene set.

TYPES OF MMA

MMA can be caused by several enzymes that are not functioning normally. The different types of MMA are described by the enzyme that is affected.

Methylmalonyl CoA Mutase (MCM) Deficiency is a type of MMA that occurs when the MCM enzyme does not function at all or does not work well enough to prevent organic acids from building up.

"Vitamin B12 responsive" MMA. In the body, Vitamin B12 (or cobalamin) is changed by a series of enzymes to compounds called cobalamins, with different forms of cobalamin used as "co-factors" for other enzymes to function. This type of MMA results when not enough adenosylcobalamin is made for the MCM enzyme to work properly. It causes symptoms similar to those of MCM deficiency, but can be treated by giving vitamin B12 (cobalamin) supplements.

Methylmalonic Acidemia + Homocystinuria (MMA + HCU) results when the body is not able to use vitamin B12 correctly. This causes homocysteine, methylmalonic acid, and other harmful substances to build up in the blood. The most common form is called Cbl C deficiency. Most babies show symptoms for Cbl C deficiency within the first year. Most children with this deficiency receive vitamin B12 injections along with their diet. Please refer back to Figure 2 for more details.

DIAGNOSIS OF MMA

Most states require all babies to be screened for MMA and other conditions before they are discharged from the hospital. In cases where MMA is not tested in newborn screening, an infant may be diagnosed after showing symptoms of the condition.

If the initial screening tests show that a baby may have MMA, 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 MMA.

SYMPTOMS OF MMA

Excessive ILE, MET, THR, VAL, and methylmalonic and propionic acid in blood and tissues affect the nervous system. Newborns with severe disease typically show symptoms within the first days of life. Children with mild or moderate disease may not show symptoms until early childhood. These symptoms may be brought on by illnesses or even exhaustion. An infant or child who is untreated, ill, or in poor control may have some or all of these symptoms:

- Anorexia (refusal to eat)
- Irregular muscle movement
- Poor sucking ability
- Vomiting
- Dehydration
- Lethargy (excessive tiredness or sleepiness)
- Metabolic acidosis (excess acid in the blood)
- Respiratory difficulty (unusually rapid breathing)
- Hypotonia (poor muscle tone)
- Seizures

Children who have a combined deficiency type of MMA, such as Cbl C, sometimes develop symptoms later in infancy. They may have more severe neurological problems including microcephaly (small head) or hydrocephalus (fluid in the cavities of the brain). They may also develop poor liver function, certain types of anemia (low iron), and visual problems.

TREATMENT OF MMA

The treatment your child receives depends on how old she was when diagnosed, how much MCM activity is present, and how she responds to therapy. The two main goals of treatment in a patient who is critically ill are to remove the toxic substances that have built up and increase body protein synthesis.

During very early treatment, if test results show that vitamin B12 helps MCM work, taking large doses of this vitamin may be the only treatment needed. As the child improves, a diet high in calories but low in ILE, MET, THR, VAL, and polyunsaturated fats (PUFAs) and free of odd-chain fatty acids is prescribed. Large doses of carnitine, a substance that increases the elimination of propionic acid from the body, are also given.

Additional Therapies: Certain vitamins or medications for your child with MMA may be recommended by your metabolic doctor.

- **Vitamin B12** is used to treat cobalamin-responsive and combined-deficiency MMAs. Some children respond to oral cyanocobalamin supplements, but other children must receive only the hydroxocobalamin given by injection.
- **Betaine** is a medication that may be given to children with MMA Cbl C to reduce the homocystine levels in the blood.
- **Carnitine** is a nutrient that helps energy enter cells in the body. Carnitine can also bind with toxic substances and help the body get rid of them.
- **Metronidazole** (me-troe-ni-da-zole) (Flagyl®) is an antibiotic that may be given to reduce the amount of propionate that is produced by bacteria in the gut. Other antibiotics may be used for this purpose as well.

Constipation can be a common problem in MMA, and medications to increase gut functioning are often used. Your metabolic doctor will decide what medications are appropriate and prescribe them in doses based on your child's individual needs. It is important to use only the exact medications your doctor prescribes, as other forms may not be effective.

NUTRITION SUPPORT OF MMA

A diet that reduces ILE, MET, THR, VAL, and odd-chain fatty acid intake is used to help prevent most of the symptoms of MMA. This diet, which is different for each person with MMA, can lower the blood of ILE, MET, THR, and VAL 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.

Protein. Many foods contain protein. Those foods also contain ILE, MET, THR, and VAL. Your child with MMA must limit the amount of foods that contain protein. Table 1 is a general guide to foods that are not allowed, foods that are limited, and foods that may be eaten freely if obesity is not a problem.

Odd-Chain Fatty Acids. Food fats that contain fatty acids with an uneven number of carbons are called odd-chain fatty acids. These fats produce some propionic acid when they are used in the body. Food fats that contain a small amount of oddchain fatty acids include butter, chicken fat, cream, some fish oils, lard, and olive oil. These foods may be restricted for your child. Avoidance of fasting is also very important, as fasting leads to a build-up of odd-chain fatty acids.

PUFAs. Vegetable oils such as canola, corn, safflower, and soy contain large amounts of polyunsaturated fatty acids (PUFAs). According to some reports, when large amounts of PUFAs are eaten, a small portion of each PUFA is broken down to propionic acid. Not everyone agrees with these reports. However, until more is known on this topic, the best approach is to limit vegetable oils that are high in PUFAs to the amount required to provide essential fatty acid(s). Coconut oil, palm oil, and peanut oil are low in PUFAs and may be used as energy (calorie) sources. Ask your metabolic doctor or dietitian which is best for your child.

Requirements for ILE, MET, THR, VAL, Protein, and Energy. A child with MMA who eats enough protein to grow properly gets too much ILE, MET, THR, and VAL. 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, fruits, fats, vegetables, and sweets. Eating these foods in the amounts needed to provide just enough ILE, MET, THR, and VAL does not provide enough protein to meet your child's needs for growth.

To get enough protein for growth and not get too much ILE, MET, THR, and VAL, a special medical food that is high in protein but contains no MET or VAL and is low in ILE and THR is necessary.

To be sure your child is getting enough energy and protein, as well as adequate amounts of ILE, MET, THR, and VAL for growth and development, the nutritionist carefully calculates the amount of each nutrient needed. Too little ILE, MET, THR, VAL, protein, or energy can result in growth failure. Frequent diet adjustments are necessary, especially during the first year of life when babies grow rapidly. The nutritionist or metabolic doctor will make these diet changes based on your child's health, growth, dietary intake, and lab tests.

Propimex®-1 Amino Acid-Modified Medical Food With Iron is a medical food used to provide protein for infants and toddlers with MMA. Propimex-1 contains very little ILE and THR and no MET or VAL. Similac Advance Infant Formula with Iron, breast milk, or other intact protein **must** also be fed to provide the specific amount of ILE, MET, THR, and VAL your baby needs for growth and development. Breast milk is lower in ILE, MET, THR, and VAL than infant formula or cow's milk and can be used to supply the required amino acids. 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 infant's medical food. Propimex-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.

Propimex®-2 Amino Acid-Modified Medical Food is a medical food used in treating children and adults with MMA. Propimex-2 contains no MET and VAL and little ILE and THR, so some whole protein containing these amino acids **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 the amounts your child can eat. **Propimex-1 and Propimex-2 are to be used under medical supervision.**

Table 1. General Guide to Foods on ILE, MET, THR, and VAL-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 other seafood, meat, nuts, nut butters, poultry, seeds, tofu	Breast milk, infant formulas, 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

Propimex-1 and Propimex-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 Propimex is very important, and they should not emphasize the difference in taste or odor between milk and medical food to the child with MMA.

Most children taking medical foods for MMA 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 Propimex at first, but in time accept it.

Flavorings, such as Kool-Aid® Unsweetened Soft Drink Mixes, Wyler's® Unsweetened Soft Drink Mixes, and concentrated fruit juices can be added to Propimex. Propimex 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. However, the best way to be sure your child is getting the proper amounts of ILE, MET, THR, and VAL is to weigh foods on a scale that reads in grams.

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)

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 the 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 Propimex 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 MMA is the same as for any baby. The Propimex formula will be supplemented with breast milk or infant formula such as Similac Advance EarlyShield. The nutritionist may have you mix the two formulas together. The Propimex 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 Propimex-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 Propimex 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.

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.

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

Propimex-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 ILE, MET, THR, and VAL with another food, and write it down.

When your child is older, the differences between the MMA-restricted diet and the diets of other children will be greater.

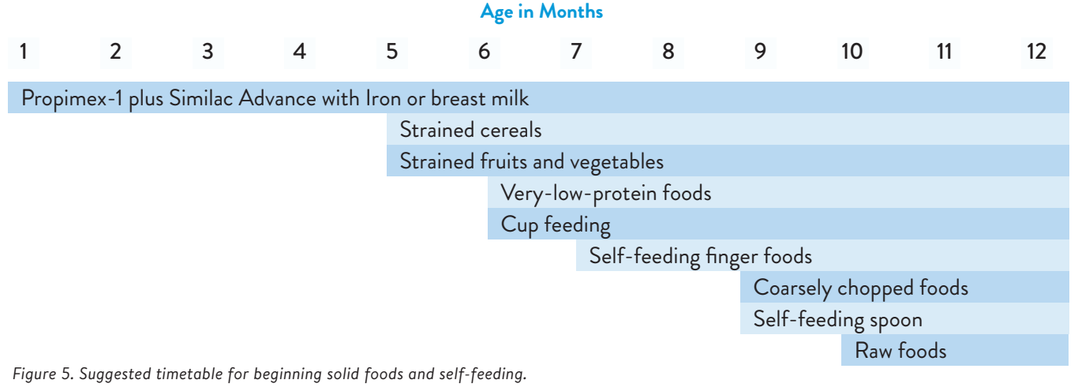


Figure 5. Suggested timetable for beginning solid foods and self-feeding.

Your child with MMA will require Propimex 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 his energy needs. Free foods, which are high in energy and contain little or no ILE, MET, THR, and VAL, must not replace prescribed foods nor be used in large amounts. If your child eats too many of these free foods, he 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 have questions about the content of certain foods, 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 protein.

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 MMA is controlled, and to indicate if changes in treatment are needed. Your doctor may ask for blood and urine tests frequently in the first year of life. After 1 year of age, blood and urine will be checked less frequently if blood ILE, MET, THR, VAL, and organic acid levels are well controlled. How often your child is tested will be determined by her metabolic doctor.

Urine may be monitored for the presence of organic acids and their toxic substances. When a child is not getting enough calories or is ill, his body fat is broken down for energy. Ketones, made from excess use of body fat for energy may be detected in the urine. The clinic may provide you with test strips (Ketostix®) that measure the level of ketones in the urine. The presence of ketones in the urine may indicate that your child is not getting enough calories.

Before taking a blood sample, you may be asked to accurately record your child's total food and beverage intake. On a form the clinic will provide, record the name of the food, the exact amount in household measures (cups, teaspoons, or tablespoons) or in grams that your child ate, and the protein 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 results.

ILE, MET, THR, and VAL Levels. The amount of ILE, MET, THR, and VAL in the blood is an indirect measure of how much ILE, MET, THR, and VAL are present in body tissues. Of most concern is the brain, because too much methylmalonic and organic acid, ammonia, as well as too little sugar, are harmful to brain development. Because blood transports nutrients to the brain, the concentration of ILE, MET, THR, VAL, 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 ILE, MET, THR, and VAL levels that are **high** may indicate that your child is eating more foods that are high in protein than his body needs for growth. Illness, such as colds and flu, can also cause the body to break down its own protein, releasing these amino acids into the blood. When your child is not getting enough protein, because of rapid growth or inadequate intake of the medical food, the blood levels may also rise. Initially during rapid growth, blood levels will decrease and then increase again as the body breaks down its own protein.

Low ILE, MET, THR, and VAL levels usually indicate that your child is not getting enough protein in the diet.

Clinic Visits. Because MMA 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 the 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 may be made, if needed, and any questions you may have will be addressed.

In addition to the metabolic specialist, you should have a family doctor to provide required ongoing well-child care. This doctor should give immunizations at 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 MMA whose intake is well controlled and whose diet supplies adequate nutrients should grow as well as a child without MMA.

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 Propimex-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, Propimex may taste different

when taken from a cup instead of a bottle. Also, the smell of Propimex 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 Propimex 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 Propimex 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 PROPIMEX® 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 Propimex 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 MMA 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 MMA. Some materials that you may find helpful are listed on page 17.

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. Your dietitian may provide you with a technique or way to count protein that you can teach your child.

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 protein in foods. As your child gets older, she should understand what blood levels of ILE, MET, THR, and VAL are considered normal and the consequences of high levels.

Adolescence. Adolescence may be a difficult time for both you and your child, regardless of MMA! The influence of friends and the struggle for independence may make dietary compliance a challenge. Teens may feel that MMA 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 MMA would rather tell people they are vegetarian or vegan than explain about MMA. Help your teenager deal with her peers and not be self-conscious that she has MMA. Finding a peer with MMA through a support group 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 MMA 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 Propimex, which may depress the appetite for other foods; or having lower than normal amino acid blood levels. Medications may also decrease appetite. Some children have a poor appetite despite adequate treatment and dietary management. In such cases, it may be necessary to use a feeding tube to ensure nutrition needs are met.

Unusual Hunger. This may be an indication that the diet needs to be adjusted. The amount of Propimex 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 Propimex because of normal variations in appetite, and this should not be of concern if average intake over a week is adequate. If Propimex is not offered regularly, a child may decide to refuse it. Improperly mixed Propimex also can cause refusal—too much water makes the volume too great; too little water makes the Propimex mixture too thick. A child may refuse Propimex as an attention-getting device, especially if he senses that his parents are anxious for him to drink the Propimex mixture. Remember, Propimex 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. Food jags and strikes are common among young children. The prescribed amount of Propimex 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."

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 Propimex 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 ILE, MET, THR, and VAL-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, blood 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 Propimex.

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 Propimex 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 MMA

Parents carry the bulk of the responsibility for managing their child's MMA. 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 MMA, 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 MMA 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 MMA because he is on a special diet. Treat your child with MMA as normally as possible.

Grandparents love to spoil their grandchildren! It may be difficult for them as they sometimes feel the child with MMA 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 MMA 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 and fat breakdown needs to be prevented in children with MMA because it will release too much ILE, MET, THR, VAL, and organic acids into the blood. ILE, MET, THR, VAL, 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 MMA 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 Propimex, especially if your child is nauseated or vomiting. Soda crackers may be the only food she will feel like eating. Encourage intake of any allowed foods that your child is willing to eat.
- Encourage your child to continue drinking her medical food if she 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; sugar-sweetened carbonated beverages; Kool-Aid®; Tang®; tea with sugar; vegetable broth; or fruit juices with some sugar added.
- Dilute the Propimex 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 MMA 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..

A LOOK TO THE FUTURE

Continuing the Diet. MMA 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 MMA diet may cause mental and nervous system damage at any age. Metabolic doctors and nutritionists provide support that is essential for helping your child have a normal, productive life.

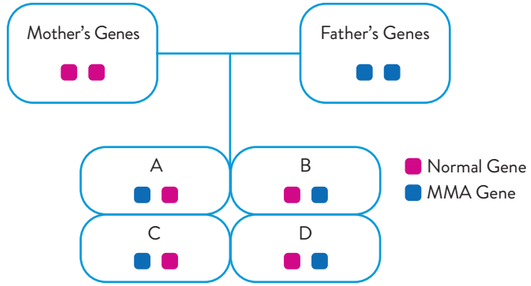


Figure 6. All children of a person with MMA and a person who doesn't have MMA will be carriers of MMA.

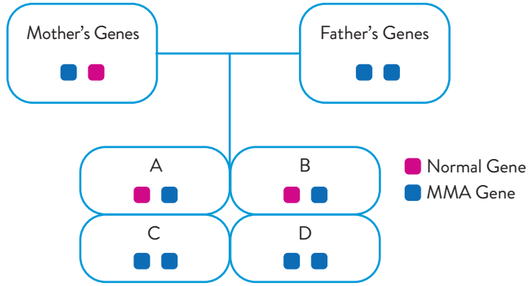


Figure 7. Approximately half of the children of a parent with MMA and a parent who is a carrier of MMA will have MMA.

Family Planning. The chance that two carriers of MMA will have a child with MMA is 1 in 4, or 25%, for each pregnancy (Figure 4). Because you have a child with MMA, you know that both parents are carriers. That means you have a 25% risk with each pregnancy of having another child with MMA. 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 MMA plan to have any more children, they should take time to seriously think about the special parenting tasks that parents of a child with MMA 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 MMA 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 having 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 MMA before having another child.

Offspring of a Person with MMA. All children born to a person with MMA will be carriers of the gene or have MMA. As shown in Figure 6, all offspring of a parent with MMA (●●) and a parent who is normal (●●) inherit one normal (●) and one MMA (●) gene. Each one of their children will be a carrier.

If a person with MMA has children with a carrier for MMA, approximately one-half (50%) of their offspring will have MMA and one-half (50%) will be carriers (Figure 7).

Childbearing by Women with MMA. For the woman with MMA, having children may cause problems. A major concern for MMA 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. For women with MMA, there is the strong possibility of damage to an unborn child if the mother is not on diet during pregnancy. Infants born to women with untreated MMA may have mental retardation and other birth defects.

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

Kool-Aid®-Flavored Propimex®-1

Yield: 8 fl oz

40 g Propimex-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*
Isoleucine, mg	6	48
Methionine, mg	0	0
Threonine, mg	5	40
Valine, 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 Propimex®-2

Yield: 8 fl oz

20 g Propimex-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*
Isoleucine, mg	48	57	76
Methionine, mg	0	1	13
Threonine, mg	40	60	69
Valine, mg	6	20	20
Protein, g	6.5	6.7	8.5
Energy, kcal	257	276	251

1, Concentrated fruit "drinks" do not contain any protein (valine). Substitute when available.
[1]Please check with your dietitian or doctor before using this recipe in infants.

Kool-Aid®-Flavored Propimex™-2

Yield: 16 fl oz

40 g Propimex-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*
Isoleucine, mg	96
Methionine, mg	0
Threonine, mg	80
Valine, 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 Propimex Medical Food

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

Use low-protein food lists to calculate protein 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: _____

_____

Your Path to Insurance Reimbursement Support

pathway plus

Abbott offers a reimbursement support program to help determine your coverage options for Abbott Metabolic products and will connect you with a supplier who can help get it delivered right to you door.

How it works

STEP 1 **You Call** with patient's information, insurance and diagnosis

STEP 2 **We Help** determine available coverage options

STEP 3 **We Connect** your covered patients to a supplier

Call To Get Started: 1-855-217-0698 (M-F, 8:30 a.m. to 5:00 p.m. EST)

To learn more, visit **www.pathway-plus.com**

Abbott Metabolic Medical Foods

21 products to meet a wide range of nutrition needs in more than 40 inborn errors of metabolism.

Phenylketonuria (PKU)

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

Propimex® is part of an extensive
line of medical foods from
Abbott, makers of Similac®

20202993/July 2020
LITHO IN USA

Abbott