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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

Tyrosinemia Type I

CONTENTS

Abbott provides this booklet to health care professionals to help them counsel families, and to families to help them learn about TYR-1.

INTRODUCTION TO TYROSINEMIA TYPE 1

Your child has a condition called Tyrosinemia (ti-ro-sin-e-me-a) Type I (TYR-1). Children who have inherited this disorder cannot use the amino acid tyrosine (ti-ro-seen) (TYR) in a normal way. TYR is an amino acid that 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 TYR 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 to answer them.

WHAT IS TYR-1?

TYR-1 is an inherited disorder of amino acid metabolism. Proteins, which are made up of amino acids, are found in many parts of the 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. Tyrosine (TYR) is one of these amino acids. All foods with protein contain TYR. High-protein foods are dairy products, dried beans and peas, eggs, meat, poultry, nuts, soy products, seafood, seeds, and peanut butter. Fruits, grains, and vegetables have less protein and, therefore, have less TYR. These are allowed in the diet in measured quantities.

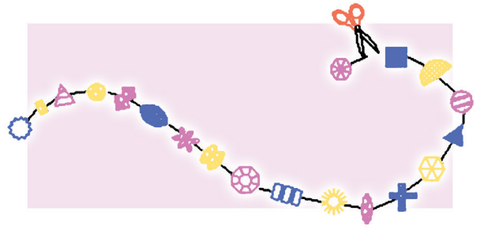


Figure 1. Amino acids are joined together like beads on a necklace to form protein. Enzymes act like scissors to remove amino acids from protein.

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 TYR is split off from food protein, it is absorbed, changed, and used to form many other useful substances in the body. Phenylalanine (fen-il-al-a-neen) (PHE)—another amino acid found in all protein foods—that is not used immediately to build new protein is changed to TYR. For the body to rid itself of the products of the breakdown of TYR, or to use excess TYR for energy, another enzyme, called fumarylacetoacetate hydrolyase (few-mar-il-a-see-to-as-atate hi-drow-lie-ace) (FAH), is required.

Some people, such as your child, do not have normally working FAH, or do not have enough to handle all the TYR that is in the protein foods they eat. In either case, TYR cannot be used normally, and TYR or the products from its

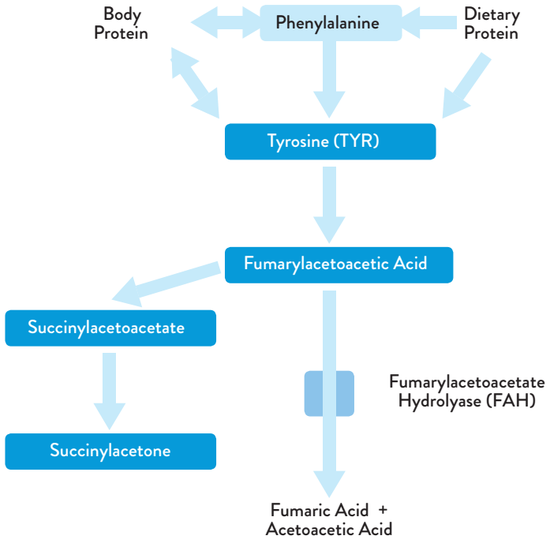
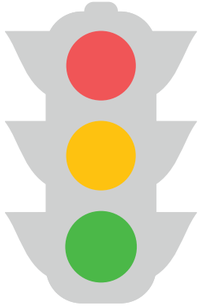


Figure 2. Metabolic pathway for TYR. Substances in the shaded boxes build up when FAH doesn't work..

breakdown build up as succinylacetoacetate (suc-sin-eel-a-see-toe-asa-tate) and succinylacetone (suc-sin-il-as-a-tone), which are extremely toxic (poisonous) substances. Figure 2 shows what happens in TYR-1.

Think of the situation as a traffic intersection (Figure 3).



FAH not working.
TYR and PHE cannot be broken down. TYR, PHE, and succinylacetone build up in blood and spill into urine.

FAH not working well.
TYR and PHE may not be broken down efficiently.

FAH working.
TYR and PHE used normally.

Figure 3. The fumarylacetoacetate hydrolyase (FAH) traffic light.

A green light (normal FAH) allows TYR and PHE to be used normally. A red light (no or too little FAH) keeps TYR and PHE from being used normally. If the light is stuck on red, a traffic jam occurs—TYR, PHE, and succinylacetone build up in blood and tissues and cause the symptoms of TYR-1. If a person with TYR-1 isn't treated, TYR, PHE, and succinylacetone also spill into the urine.

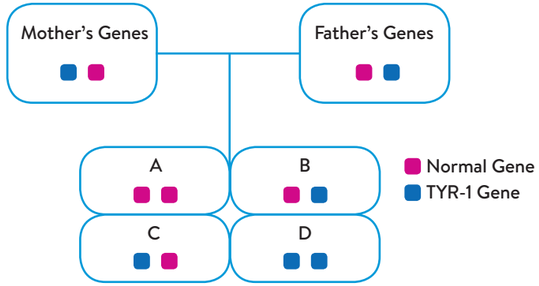


Figure 4. Genetic inheritance of TYR-1.

TYR-1: AN INHERITED DISORDER

TYR-1 is a genetic disease 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 body cell. These genes serve as blueprints, or patterns, to direct the body to make enzymes such as FAH.

Each parent of a child with TYR-1 has one normal (■) and one altered TYR-1 (■) gene. Each one of their offspring 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 FAH to use TYR 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 TYR-1 (■) gene. His body will make enough FAH to use TYR normally, but he can pass on the TYR-1 gene to his offspring. A person with this gene set—1 normal and 1 TYR-1—is called a carrier. Being a carrier does not affect the person's health. **You, as parents of a child with TYR-1, are carriers.** Brothers and sisters of your child with TYR-1 may also be carriers.

A child with gene set D has TYR-1 caused by the two TYR-1 genes (■■), one from the mother and one from the father. Her body will not be able to use the TYR in food normally. She will also pass a TYR-1 gene on to each of her offspring. Your child with TYR-1 has this gene set.

TYPES OF TYR-1

"Type 1a" is caused by a defect of FAH with production of an abnormal metabolite, succinylacetone, which is formed from the accumulated substrate fumarylacetoacetate.

- "Acute" TYR Type 1a symptoms present soon after birth. Infants develop progressive liver and kidney failure, vomiting, diarrhea, and a "cabbage-like" odor.
- "Chronic" TYR Type 1a is similar to the acute form, however, symptoms are milder and appear later in infancy. Symptoms tend to include rickets, liver and kidney dysfunction, high blood pressure, and nervous system dysfunction.

DIAGNOSIS OF TYR-1

All states require all babies to be screened for excess levels of TYR in the blood before they are discharged from the hospital. Some states require babies urine to be screened for the presence of succinylacetone. This is a more sensitive marker to diagnose TYR-1. These babies are often diagnosed in the newborn period. Sometimes babies who are screened only using blood levels of TYR are not detected until they show symptoms of TYR-1. Symptoms of liver failure and the cabbage-like body odor may lead the doctor to test the blood or urine for TYR, PHE, and succinylacetone. Often a liver biopsy will be performed. Urine tests for the presence of succinylacetone and tissue tests for FAH activity establish the diagnosis of TYR-1. Some doctors hospitalize the infant to confirm diagnosis because testing is more rapid and diagnosis and treatment can begin sooner.

SYMPTOMS OF TYR-1

With early diagnosis and lifelong nutrition support, a person with TYR-1 can develop normally if blood TYR and PHE levels are kept near normal. In untreated patients with TYR-1, the buildup of succinylacetoacetate and succinylacetone affects the nervous system and the body's ability to maintain other normal functions.

The symptoms of the acute form of TYR-1 usually appear in the first few weeks of life. An untreated infant might have some or all of these symptoms:

- failure to thrive
- vomiting
- diarrhea
- cabbage-like body odor
- liver failure leading to internal bleeding
- abnormal swelling in body cells from excess fluid
- abnormal swelling in the abdomen from excess fluids
- yellow skin color (jaundice)
- rickets (softening and bending of bones)

The chronic form of TYR-1 , which usually shows up after the first year of life, includes the symptoms listed above in milder form, as well as kidney and liver failure. Many children experience episodes of severe abdominal and joint pain and elevated blood pressure.

NUTRITION SUPPORT OF TYR-1

A diet that reduces PHE and TYR intake is used to help prevent most of the symptoms of TYR-1. This diet, which is different for each person with TYR-1, can lower the blood PHE and TYR levels to a range that may allow normal mental development and growth.

The special TYR-1 diet for your child is very important. With proper nutritional management, your child will grow and develop normally.

Many foods contain protein. Those foods also contain PHE and TYR. Your child with TYR-1 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.

Additional Therapies. Your metabolic doctor may recommend certain vitamins or medications for your child with TYR-1.

Orfadin or Nityr (nitisinone), 2-(2-nitro-4-trifluoro-methylbenzoyl)-1,3 cyclohexanedione (NTBC), is a drug that is paired with nutrition therapy for the treatment of TYR-1. Typically prescribed as soon as diagnosis is confirmed, NTBC raises the blood TYR concentration, therefore, dietary management of TYR and PHE intake needs to be controlled.

Liver transplantation is reserved for those children who have severe liver failure at diagnosis and who fail to respond to the NTBC therapy. Liver transplantation may also be considered when there is evidence of malignant changes in the liver.

Requirements for TYR, PHE, Protein, and Energy. A child with TYR-1 who eats enough protein to grow properly gets too much TYR and PHE. Foods high in protein are cheese, eggs, meat, milk, soy milk, poultry, fish, nuts, dried beans and peas, seeds, and peanut butter. Foods low in protein include some cereals, fruits, fats, vegetables, and sweets. On the other hand, eating these foods in the amounts needed to provide just enough TYR and PHE does not provide enough protein to meet the child's needs for growth. **To get enough protein for growth and not get too much TYR and PHE, a special medical food that is high in protein and free of TYR and PHE is required.**

To be sure your child is getting enough energy, adequate TYR and PHE, and sufficient protein for growth and development, a nutritionist carefully calculates the amount of each nutrient needed. Too little TYR, PHE, 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, TYR and PHE intakes, blood levels of TYR and PHE, and urinary excretion of succinylacetone.

Tyrex®-1 Amino Acid-Modified Medical Food With Iron is used to provide protein for infants and toddlers. Tyrex-1 does not contain any TYR or PHE, so Similac® Advance® with Iron Infant Formula, breast milk, or other intact protein must also be fed to your baby to provide the specific amounts of TYR and PHE she needs for growth and development. Breast milk is lower in phenylalanine and tyrosine than infant formula or cow's milk and can be used to supply the required TYR and PHE. 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. Tyrex-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.

Tyrex®-2 Amino Acid-Modified Medical Food is a medical food used in treating children and adults with TYR-1. Tyrex-2 contains no TYR or PHE, so the need for TYR and PHE **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. **Tyrex-1 and Tyrex-2 are to be used under medical supervision.**

Tyrex-1 and Tyrex-2 look and taste different from milk. 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 when 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 Tyrex is very important, and they should not emphasize the difference in taste or odor between milk and medical food to the child with TYR-1.

Most children taking medical foods for TYR-1 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 Tyrex at first, but in time accept it.

Table 1. General Guide to Foods on TYR- and PHE-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

Flavorings, such as Kool-Aid® Unsweetened Soft Drink Mixes, Wyler's® Unsweetened Soft Drink Mixes, and concentrated fruit juices, can be added to Tyrex. Tyrex 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. Be careful which pudding mixes you buy, as some contain more protein than others.

Aspartame (NutraSweet®) contains PHE and must not be used as a sweetener. Many foods and some medicines contain aspartame and should be avoided. Read labels carefully!

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 way to be sure your child is getting the proper amount of PHE and TYR 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 provide by your nutritionist or metabolic doctor.**
- Wash your hands and all supplies carefully before preparing formula.
- **Do not** mix longer than indicated on the Tyrex label.
- Overmixing causes the fat emulsion to break. Separation of the medical food mixture then occurs. Overmixing may also add air that causes destruction of 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.
- Refrigerate the medical food after mixing. Discard any unused medical food 24 hours after mixing because of nutrient loss.

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)

Feeding Your Infant. The way you feed your baby with TYR-1 is the same as for any other baby. The Tyrex-1 formula will be supplemented with breast milk or infant formula such as Similac Advance. The nutritionist may have you mix the two formulas together. Tyrex-l 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. A few drops shaken on the inside of your wrist should feel lukewarm.
- If the Tyrex-l 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 Tyrex-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.

Tyrex-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 doctor or nutritionist 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, because 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 TYR and PHE with another food, and write it down.

When your child is older, the differences between the TYR- and PHE-restricted diet and the diets of other children will be greater. Your child with TYR-1 will require Tyrex all her life to provide most of her protein, mineral, and vitamin needs.

Diet Guidelines and Food Lists. At each clinic visit, you will be given guidance that spells out in detail what your child can eat. The amount of and how to prepare the medical food mixture are listed, and the types and amounts of food that your child is allowed are 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

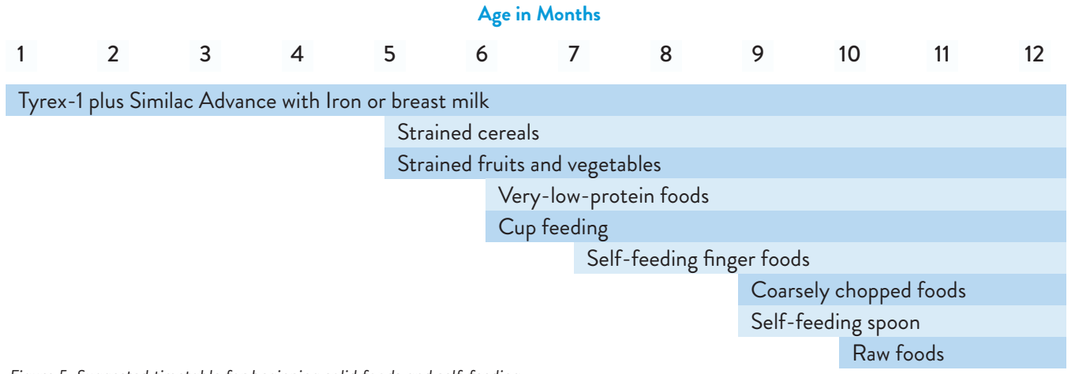


Figure 5. Suggested timetable for beginning solid foods and self-feeding.

in energy and contain little or no TYR or PHE, 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 dental caries. 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.

The nutritionist can calculate the nutrient composition of a food and help you include it in the diet plan if it is not too high in TYR and PHE.

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 his TYR-1 is controlled, and to indicate if changes in treatment are needed. Your doctor may ask for frequent blood and urine samples in the first year of life. After 1 year of age, checking blood levels and diet records may be less often if blood PHE, TYR, and succinylacetone levels are well controlled. Your baby's metabolic doctor or nutritionist will determine how often your child is tested.

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

Before taking the 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 grams or household measures (cups, teaspoons, or tablespoons) that your child ate, and the TYR and PHE 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.

TYR, PHE, and Succinylacetone Levels. Urine should be free of or contain only trace amounts of succinylacetone and other related organic acids. The amounts of TYR and PHE in the blood are indirect measures of the amounts of these amino acids present in body tissues. The body tissues of most concern are the brain, kidney, and liver, because too much succinylacetone is toxic in these tissues.

Because blood transports nutrients and other substances to and from the brain and other body organs, the concentration of TYR, PHE, and succinylacetone in the blood gives the metabolic doctor and nutritionist an idea of how much of these substances might be in the tissues. Recommended blood PHE and TYR levels vary, and your metabolic doctor or nutritionist will discuss what your child's laboratory results mean.

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

A **low** TYR and PHE level usually indicates that your child is not getting enough of these amino acids from whole protein in the diet.

Additional laboratory work may include blood and urine assessments for renal losses (bicarbonate level, potassium, and sodium), liver status (alpha-fetaprotein), and liver function tests.

Clinic Visits. Because TYR-1 is a lifelong condition that could harm your child's growth and development, you will be asked to take your child to the clinic for frequent checkups. If growth and development are normal and laboratory testing shows

good control of TYR-1, 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 TYR-1 whose PHE and TYR intakes are well controlled and whose diet supplies adequate nutrients should grow as well as a child without TYR-1.

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 growth rate usually causes a decrease in appetite.

Although the requirement for energy (calories) and protein on the basis of 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 Tyrex-1 from a cup when your child is between 5 and 8 months of age. Because tastebuds vary on different parts of the tongue, Tyrex may taste different when taken from a cup instead of a bottle. Also, the smell of Tyrex may be more pronounced in an open cup. Some mothers find a training cup that has a lid and a spout to be very useful. Offering the Tyrex at a cold temperature may also increase your child's willingness to drink from a cup.

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

During weaning, your child may not want to take all the prescribed Tyrex 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.

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 Tyrex 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 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 kg) a year, compared with 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 will 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 TYR-1 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 to your child can begin by calling allowed foods "special" or "just for you." From the time your child is very young, teach her to ask about familiar foods before eating them. As your child grows older and is able to understand the concept of a missing or nonworking enzyme, explain TYR-1. 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 vary 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 with the grocery shopping, setting the table, and preparing 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 TYR or PHE, 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 to 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 levels of TYR and PHE are considered normal and the consequences of high TYR and PHE levels.

Adolescence. Adolescence may be a difficult time for both you and your child, regardless of the TYR-1! The influence of friends and the struggle for independence may make dietary compliance a challenge. Teens may feel that TYR-1 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 TYR-1 would rather tell people they are vegetarian or vegan than explain the TYR-1. Help your teenager deal with her peers and not be self-conscious that she has TYR-1. Finding a peer with TYR-1 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 TYR-1 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 satisfies the appetite and decreases the desire to eat the foods prescribed; getting too much Tyrex, which may depress the appetite for other foods; or having lower than normal blood TYR and PHE. Medications may also decrease appetite.

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

Refusing Medical Food. A child may sometimes refuse Tyrex because of normal variations in appetite, and this should not be of concern if average intake over a week is adequate. If Tyrex is not offered regularly, a child may decide to refuse it. Improperly mixed Tyrex also can cause refusal—too much water makes the volume too great; too little water makes the Tyrex mixture too thick. A child may refuse Tyrex as an attention-getting device, especially if he senses that his parents are anxious for him to drink the Tyrex mixture. Remember, Tyrex 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 (nasogastric or gastrostomy tube) may need to be considered.

Refusing Solids. A child may experience normal variations in appetite or taste for certain foods. Or, the prescribed amount of Tyrex 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."

When your child refuses to eat, offer food at the 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 Tyrex 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 PHE- and TYR-restricted diet. The nutritionist can help you during this trying time, so do not hesitate to call. It is also very important for parents to support each other in managing a food strike. If a child is allowed to eat foods not on the diet, blood PHE and TYR 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 Tyrex supplies most of your child's nutrient needs.

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, a delay in teaching the child to drink Tyrex 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 selffeed, but this is normal. Keeping food records will help the 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 THE FAMILY AND OTHER CARE PROVIDERS IN MANAGING TYR-1

Parents carry the bulk of the responsibility for managing their child's TYR-1, so they should try to share in preparing meals and monitoring the child's diet. Other children in the family, as well as the child with TYR-1, should learn about the diet as soon as they are old enough to understand it. Older brothers and sisters should be encouraged to feed the child with TYR-1 so they become familiar with foods allowed and excluded. Make sure they understand the importance of the diet for their brother or sister's health. Brothers and sisters should be taught not to feel sorry for the child with TYR-1 because he is on a special diet. Treat your child with TYR-1 as normally as possible.

Grandparents love to spoil their grandchildren! It may be difficult for them as they sometimes feel the child with TYR-1 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 TYR-1 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 a 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 needs to be prevented in children with TYR-1 because it will release too much TYR and PHE into the blood (see Figure 2, page 3). The PHE is changed to TYR, and TYR is changed into succinylacetone and carried to the brain and other body organs where it 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 the TYR-1 child can be very serious. Your metabolic doctor or nutritionist will help you decide on how to manage it. It is essential to contact your metabolic doctor immediately if your child is unable to tolerate his medications during an illness. 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 Tyrex, 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.
- 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 Tyrex mixture, or use liquid Jell-O® if 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.

A LOOK TO THE FUTURE

Continuing the TYR-1 Diet. TYR-1 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 TYR-restricted diet may cause 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. TYR-1 occurs about one time in every 100,000 live births. People have been reported with TYR-1 throughout the world. In Quebec, Canada, the incidence is one in every 16,000 live births, and in Saguenay-Lac Saint-Jean (a region of Quebec), it is one in every 1,846 live births. In Norway, the birth prevalence is estimated to be one in 60,000.

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

Before a couple who has a child with TYR-1 plan to have any more children, they should take time to seriously think about the special parenting tasks that parents of a child with TYR-1 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 TYR-1 before a pregnancy, prenatal testing for TYR-1 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 they decide to have another child, they should give themselves time to adjust to the special needs of the first child. Parents will want to be skilled in diet management for TYR-1 before having another child.

Offspring of a TYR-1 Person. All children born to a person with TYR-1 will be carriers of the gene or have TYR-1. As illustrated in Figure 6, all offspring of a parent with TYR-1 (●●) and a parent who is normal (●●) inherit one normal (●) and one TYR-1 (●) gene. Each one of their children will be a carrier. Because the incidence of TYR-1 carriers is approximately 1 in 100–150, the possibility of a person with TYR-1 and a carrier mating and having children is small. If a person with TYR-1 has children with a carrier for TYR-1, approximately one-half (50%) of their offspring will have TYR-1 and one-half (50%) will be carriers (Figure 6).

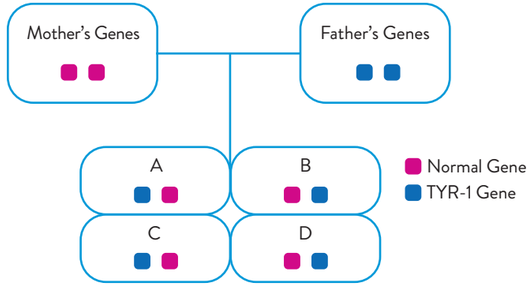


Figure 6. All children of a person with TYR-1 and a person who doesn't have TYR-1 will be carriers of TYR-1.

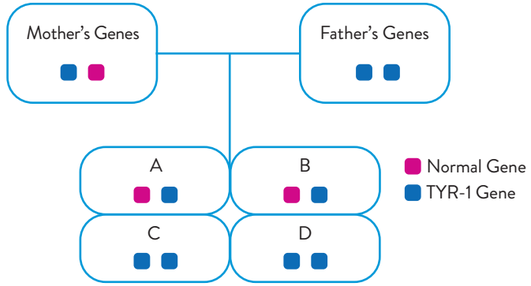


Figure 7. Approximately half of the children of a parent with TYR-1 and a parent who is a carrier of TYR-1 will have TYR-1.

Childbearing by Women With TYR-1. For the woman with TYR-1, having children may cause problems. A major concern for TYR-1 women is the stress of a pregnancy on their metabolic control. Their nutritional requirements can rapidly change during the course of a pregnancy. Pregnant women must be carefully monitored for their own safety, as well as for the health of their baby.

TYR and PHE are actively transported across the placenta. If a woman conceives while her blood PHE and TYR levels are high, mental retardation and birth defects may occur in the fetus before the pregnancy has even been confirmed. If a woman with TYR-1 is not on a TYR- and PHE- restricted diet during the duration of the pregnancy, then the baby is also exposed to the increased concentrations of these metabolites. Prolonged high TYR and PHE levels have a high risk of causing low-birth-weight babies, and a majority of these infants have mental retardation and birth defects.

If a woman with TYR-1 who is not on a restricted diet decides to become pregnant, she should go back on diet three to six months before becoming pregnant. Reducing blood levels of PHE and TYR to near normal may help prevent complications in her unborn child. Throughout pregnancy, the mother-to-be's blood PHE and TYR levels should be maintained near normal and her diet evaluated regularly. Successful pregnancies require attentive diet monitoring during the prenatal, labor, delivery, and postpartum periods.

Kool-Aid®-Flavored Tyrex®-1

Yield: 8 fl oz

40 g Tyrex-1
3 Tbsp, **level**, sugar[1]
1/2 tsp Kool-Aid or Wyler's® **Unsweetened** Soft Drink Mix
Do not use mixes that contain NutraSweet® or aspartame.

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*
Phenylalanine, mg	0	0
Tyrosine, mg	0	0
Protein, g	0.75	6.0
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 Tyrex®-2

Yield: 8 fl oz

20 g Tyrex-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*
Phenylalanine, mg	15	15	30
Tyrosine, mg	9	3	15
Protein, g	6.5	6.7	8.6
Energy, kcal	257	275	252

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

Kool-Aid®-Flavored Tyrex™-2

Yield: 16 fl oz

40 g Tyrex-2
3 Tbsp, **level**, sugar[1]
1/2 tsp Kool-Aid or Wyler's **Unsweetened** Soft Drink Mix[2]
Do not use mixes that contain NutraSweet® or aspartame.

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*
Phenylalanine, mg	0
Tyrosine, mg	0
Protein, g	12
Energy, kcal	293

[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 Tyrex Medical Food

- Add chocolate or strawberry syrup.
- Mix Tyrex with fruit to make a "smoothie."
- Freeze flavored medical food into "slushies" or "popsicles."
- Add dry Tyrex 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

Network of Tyrosinemia Advocates
Website: www.notacares.org

Children's PKU Network
3306 Buman Rd.
Encinitas, CA 92024
Phone:858-756-0079
Fax:858-756-105
E-mail: pkunetwork@aol.com
Web site: www.pkunetwork.org

National PKU News
PO Box 43552
Montclair, NJ 07043
Phone: 973-619-9160
EMail: info@pkunews.org
Web site: www.pkunews.org

How Much Phe
Email: support@howmuchphe.org
Website: www.howmuchphe.org

National PKU Alliance (NPKUA)
PO Box 1872
Eau CLaire, WI 54702
Phone: 715 - 495-4008
Fax: 715-713-0138
Web site: www.npkua.org

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)

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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

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

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