


New Parents'

GUIDE
TO



**TYROSINEMIA
TYPE 1**

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Preface



The purpose of this booklet is to help to familiarize you, as new parents, with tyrosinemia and its treatment.

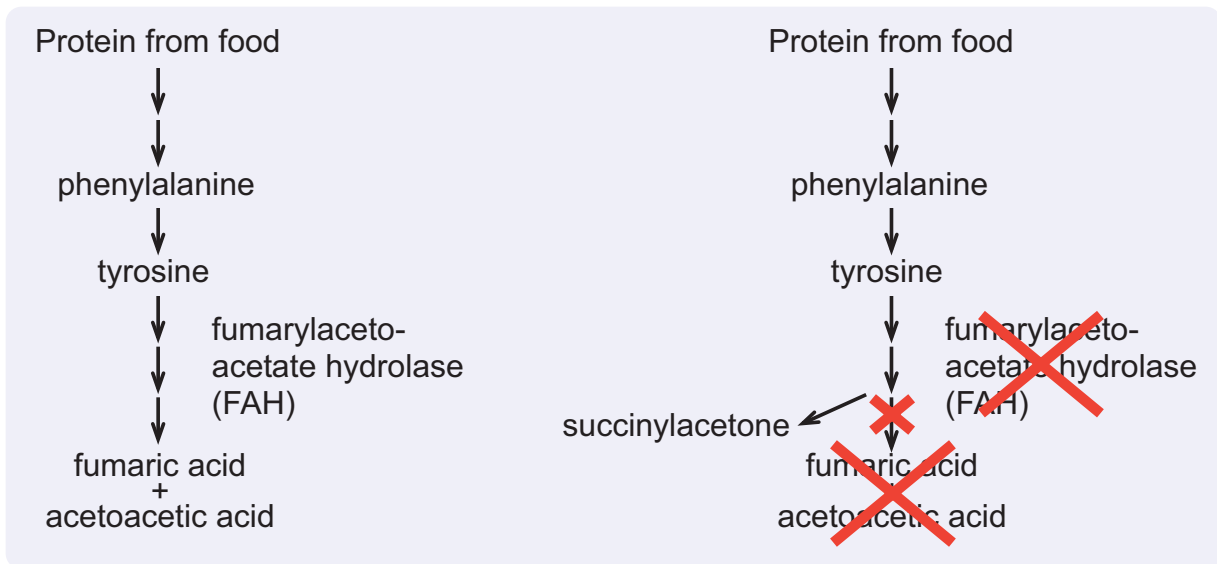
A short glossary at the end of this booklet will help you learn the vocabulary surrounding tyrosinemia. The bold blue words can be found in the glossary.



What is tyrosinemia, type 1?

Tyrosinemia (pronounced tie-roh-sin-ee-me-uh) is a **genetic** disorder in which the child is born without the ability to break down a certain chemical (amino acid) in the body. Amino acids are the building blocks of protein. One **amino acid** is called **tyrosine** (pronounced tie-roh-seen). Since this **amino acid** cannot be completely broken down, it builds up in the blood. When **tyrosine** is broken down, **succinylacetone** (pronounced suck-sin-eel-a-se-tone) is formed. When **succinylacetone** builds up in the blood, it can cause liver failure, kidney failure, and neurological problems.

Another amino acid, phenylalanine (pronounced fen-il-al'-uh-noon), is converted to tyrosine. Thus, to minimize the build up of tyrosine, children with tyrosinemia need a diet that is low in tyrosine and phenylalanine



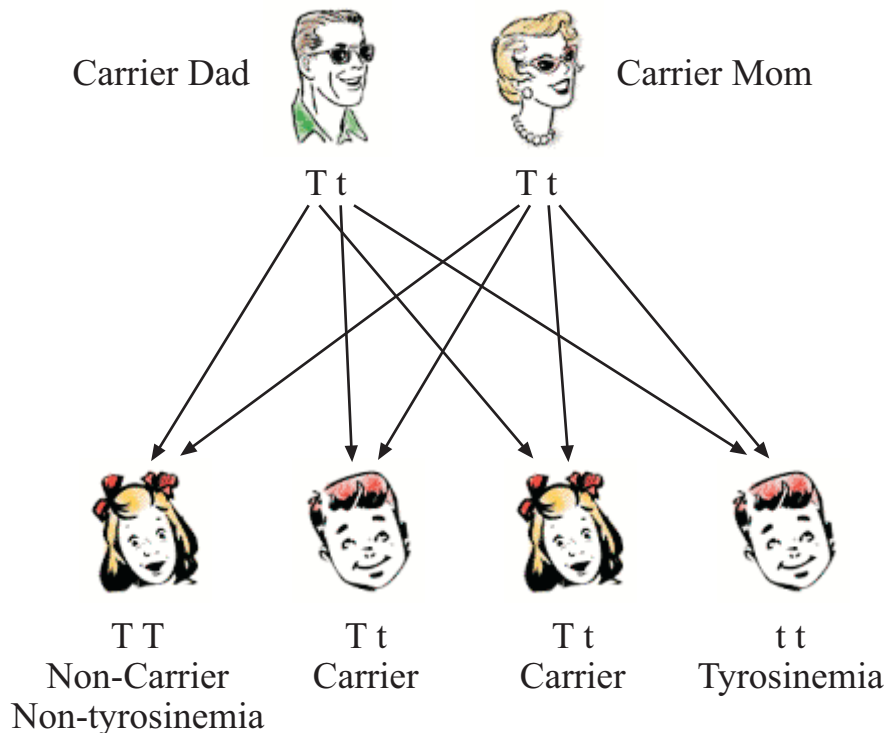
The figure above depicts the breakdown of protein to tyrosine. The figure on the right depicts the pathway for people with tyrosinemia. People with tyrosinemia do not have the enzyme FAH, so cannot convert one of the products of tyrosine into fumaric acid + acetoacetic acid. Instead, it is converted to succinylacetone

Fortunately, if the child is **diagnosed** very early and if the **blood tyrosine** and **succinylacetone** levels are kept in good **control** throughout the child's life, then severe complications can be prevented. There are other brochures that explain **tyrosinemia** in further detail, and you will be able to read through these in the future.

Tyrosinemia, type 1 is one type of **metabolic disorder**. There are also other types of tyrosinemia. In this booklet, the term "tyrosinemia" refers to **tyrosinemia, type 1**.

Where does tyrosinemia come from?

Tyrosinemia is a **genetic** condition. Individuals with tyrosinemia have received two non-working copies of the gene for tyrosinemia. One copy is passed on from each parent. This means that the enzyme (fumarylacetoacetate hydrolase) cannot work properly and the tyrosine cannot be completely broken down. Individuals who receive just one non-working copy of the tyrosinemia gene are called carriers. The normal copy of the tyrosinemia gene makes enough enzyme that they do not have symptoms of tyrosinemia and never need a low-tyrosine, low-phenylalanine diet.



When both parents are carriers, they each have a 50% chance of passing on their non-working gene. In every pregnancy there are four possible outcomes: not a carrier, not affected with tyrosinemia (25% chance), carrier by mom or by dad (50% chance), and affected with tyrosinemia (25% chance).

How is tyrosinemia treated?

Tyrosinemia is treated by lifelong management of blood tyrosine and succinylacetone levels. This probably sounds overwhelming at first, and it does mean that there is a lot to learn, but it will probably not take any longer to learn how to care for your baby with tyrosinemia than it does to learn how to take care of any new baby for the first time. It is important to realize that a baby with tyrosinemia is a normal infant whose only unique needs are for medication and a special diet. Both you and your child will start learning about the tyrosinemia diet as early as possible to ensure normal growth and development. Since your child will be learning about tyrosinemia management from the very beginning and *since this is the only diet your child will know, it will seem normal and natural.*

Tyrosinemia is treated by medication and a special diet for your child's life. The medication is called **nitisinone** (Orfadin®). Your child will take this medication twice a day. You will learn more about the special diet soon.

There are many laboratory measures that require monitoring, especially at first. In order to get to know your baby's individual needs, the doctor does frequent blood tests to measure your child's liver and kidney function and the amount of tyrosine and succinylacetone in your baby's blood. This helps the doctor and the nutritionist determine the prescription for the amount of medication and for the special formula your baby will need. At first the blood tests may be as often as once a week, but once the blood levels have stabilized then the test is done less frequently, usually once a month during infancy, and then once every three months. Your child's urine will also be tested, to measure succinylacetone.

As your child grows older the blood test will help to monitor dietary and medication compliance.





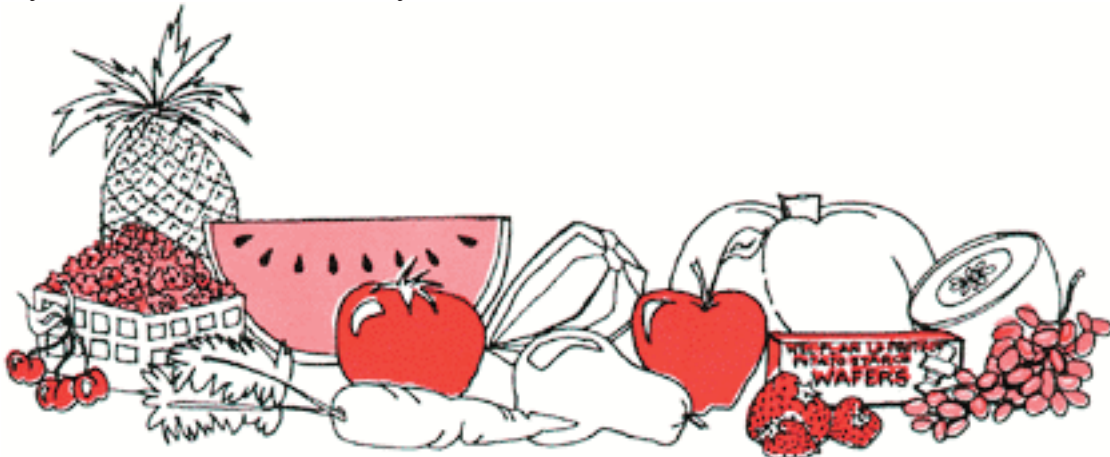
Controlling blood tyrosine

At this point, you may be wondering how to keep the tyrosine levels down to a safe level. Since tyrosine and phenylalanine are part of protein and must be eaten in order to get into the body, simply controlling the amount of protein your child eats is enough to keep the blood tyrosine levels within a healthy range.

High protein foods are also high in tyrosine and phenylalanine, so foods like milk, meat, poultry, fish, eggs, cheese, nuts, and beans are omitted from the low-tyrosine, low-phenylalanine diet. You will be learning the special food pattern along with your child as new foods are gradually added to the diet. We know which foods are highest in tyrosine and phenylalanine and which are lowest, so it is possible to choose the low-tyrosine and low-phenylalanine foods once one is familiar with them.

Since children, and especially babies, need protein in order to grow and develop normally, special foods have been developed to replace the high protein foods. The first of these products with which you will become familiar is a milk substitute. Examples of the milk substitute are:

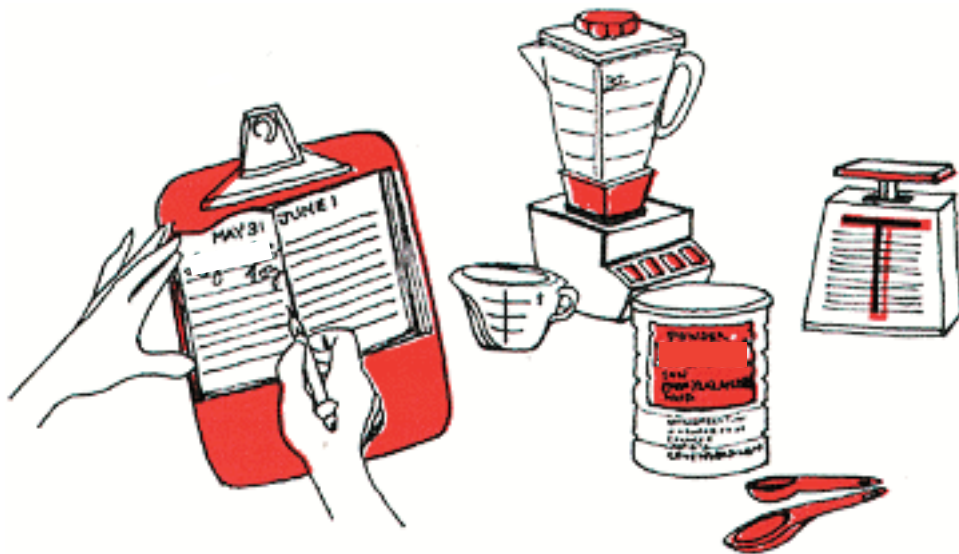
- TYROS 1[®], manufactured by Mead Johnson Nutritionals, Evansville IN
- Tyrex-1[®], manufactured by Ross Products Division, Columbus, OH



Specialized formula

TYROS 1[®] and Tyrex-1[®] are special formulas designed specifically for babies with tyrosinemia. They contain all the needed protein and other nutrients, including vitamins and minerals, that a growing baby needs, but have limited amounts of tyrosine and phenylalanine. The formula is a "super food" and will be the main source of nutrients for your baby.

The term "medical food" is also used to describe your child's specialized formula.



If you are new parents, then learning to prepare the low-tyrosine, low-phenylalanine formula will be just as easy as learning to prepare other baby formulas. Over the first few weeks the doctor and nutritionist are adjusting the formula in order to stabilize your baby's blood tyrosine levels, so the prescription (recipe) may be changing frequently at first. The prescription and formula preparation will soon become easy to follow. It is very important to measure everything accurately to make sure that your baby is getting exactly the right amount of nutrients, tyrosine, and phenylalanine.

Although practice varies from clinic-to-clinic, in most cases you will be given a prescription or recipe for enough formula for 24 hours at a time. It may be written in the form of this example:

25 g TYROS 1^{®*} powder

35 g Enfamil^{®§} powder

Add water to make 15 ounces

The prescription you receive will be calculated specifically for your baby

How to prepare formula

To make your child's formula:

- A. Blender method: Using an immersion blender (e.g., Braun[®] hand blender), measure 1 cup of water and place in a large Pyrex[®] measuring bowl. Add the weighed TYROS 1^{®*} powder and blend. Add in the weighed Enfamil^{®§} powder and add enough water to give the total formula volume required. Quickly blend again. Pour into clean baby bottles and refrigerate.
- B. Shaking method: Weigh the TYROS 1^{®*} powder and place in a large pitcher with a tight cover. Add about half of the water and shake. Add the weighed Enfamil^{®§} powder and enough water to give the total volume required. Shake well until mixture is smooth. Pour into clean baby bottles and refrigerate.

To store formula: Formula should be refrigerated after preparation the same as other baby formulas. The formula should only be kept for 24 hours after being mixed. To store the opened can of powder, simply close it tightly to keep out humidity. Too much humidity can cause the powder to become caked and hard.

* or other low-tyrosine, low-phenylalanine formula, such as Tyrex-1[®]

§ or other standard, infant formula

The tyrosinemia clinic

Many children with tyrosinemia receive regular care from a metabolic or genetics clinic. (Some children may be seen regularly in other specialty or primary care clinics.) The following information describes what you may encounter if your child is followed by a clinic for children with metabolic disorders. At the University of Washington, this clinic is called the "Biochemical Genetics Clinic."

The Biochemical Genetics Clinic is made up of a team of trained health care professionals specializing in the management of metabolic disorders. You may have already met some of the team members:

The clinic physician performs needed physical and neurological exams. He/she consults with families on medical matters and monitors current research in the field of tyrosinemia. The physician will determine that the diagnosis of tyrosinemia, type 1 is correct. The physician will also prescribe your child's medication and ensure that your child receives the correct dose of medication.



The clinic nutritionist works closely with the child with tyrosinemia and the family to make sure that the child is receiving the necessary nutrients for normal growth and development while following the low-tyrosine, low-phenylalanine food pattern. At clinic, the nutritionist talks with the parents about the child's diet, blood tyrosine level and possible dietary changes.

The clinic genetic counselor works with families to help them understand and adjust to this new diagnosis. He/she may also coordinate management by arranging lab tests and other follow-up procedures. He/she is also there to answer your genetics questions and provide feedback on the results of any testing your child has had.

The clinic social worker arranges sessions with parents and children to provide extra support around parenting issues, critical stages of management, and community and financial resources.



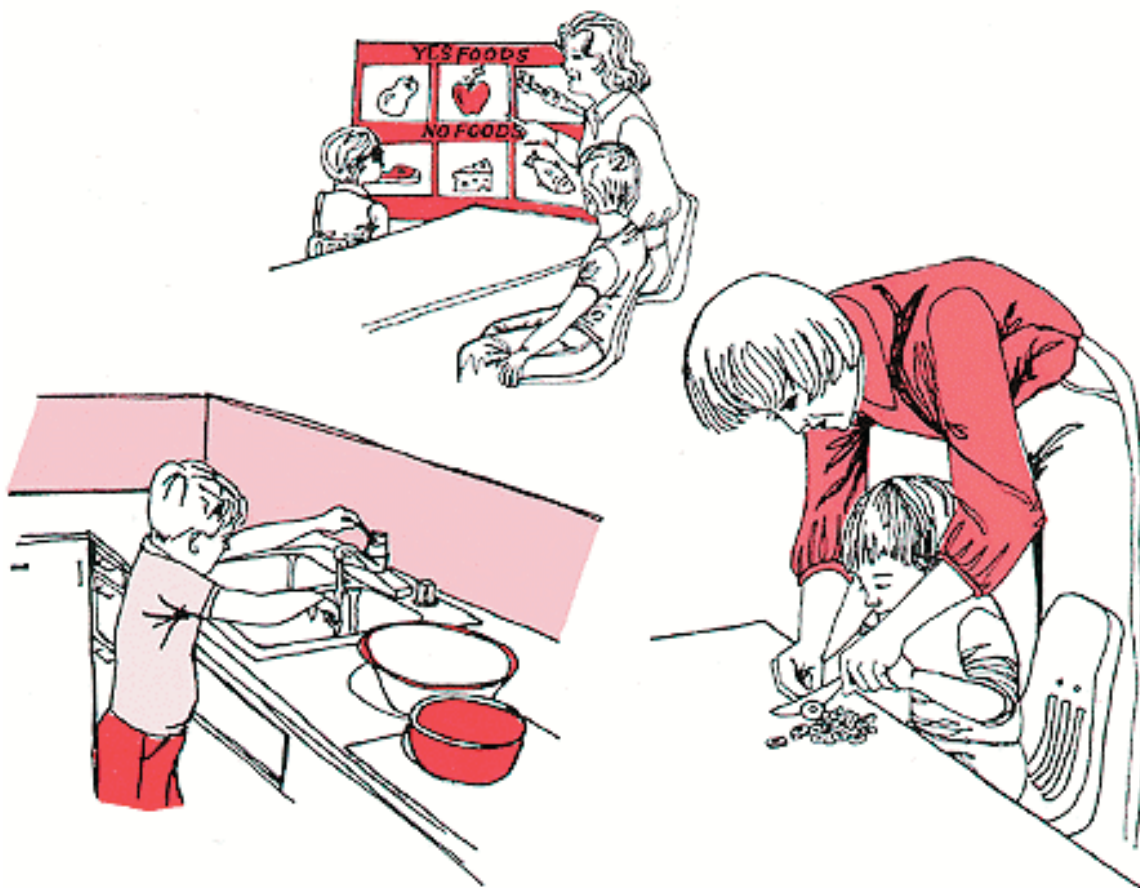
The clinic nurse screens children for developmental progress from infancy through pre-school years, monitors routine childhood medical concerns and ensures that the children's primary care medical issues are addressed in their community.

The clinic psychologist does routine psychometric testing on the children at specific ages to assess whether the children are developmentally "on schedule" and is available to evaluate those children whose parents may have concerns about cognitive or social development.

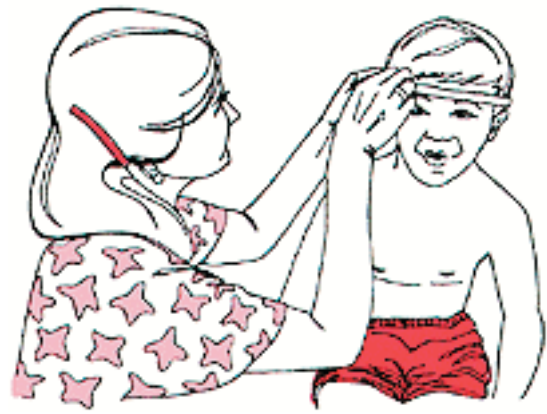
Parental Obligations

It is important that you take the management of tyrosinemia seriously to keep your infant healthy. If you are convinced that the medication and the low-tyrosine, low-phenylalanine diet are essential for your baby's good health, your child will learn to feel the same way. During infancy and childhood you are responsible for your child's compliance.





Attending the regular clinic is a very important way for the family of a child with tyrosinemia to receive support. Often, clinics can put families in contact with other families who have children with tyrosinemia or other, similar metabolic disorders. Other parents have been through similar situations with their children and can offer new perspectives that may help you resolve difficult issues.



At clinic, the child's blood tyrosine and succinylacetone levels are measured and height and weight are charted. The child is also able to participate in learning activities. The importance of regular clinic visits cannot be overemphasized.





The health of your child is dependent upon control of blood tyrosine levels and preventing the formation of succinylacetone. You as parents are responsible for your child's diet and growth and intellectual development at this early stage of life.

The clinic team is here to help you each step of the way as you strive to reach the goals of medication and dietary compliance, good control of blood levels and normal intellectual and physical development for your child.

Above all, it is important to remember that you have a healthy child who has the opportunity to develop appropriately.

Summary

The child with tyrosinemia is normal in every respect except that the child's body can only handle a small amount of tyrosine. Babies with tyrosinemia drink a milk substitute and take a specific medication to keep the blood tyrosine levels in good control and to provide the necessary nutrients for normal growth and development.



When the family and child with tyrosinemia attend clinic the child will have a blood test to measure the amount of tyrosine, nitisinone (Orfadin®), and succinylacetone in the blood and urine. Height and weight will be measured so the growth pattern can be assessed.



At clinic children are taught self-management skills so that they can make educated food choices for themselves. Older children are introduced to simple recipes that are used to demonstrate basic food preparation skills.

The ideal of "parents as teachers" is firmly upheld and encouraged at the clinic. You as parents will learn new ways to foster your child's attempts at self-management.

Glossary

Amino acid - a building block of protein. There are many amino acids but in tyrosinemia we are concerned mainly with the amino acids called tyrosine and phenylalanine

Blood tyrosine levels - (also called "serum or plasma tyrosine levels") This refers to the amount of tyrosine in the bloodstream. It is important that the level of tyrosine in the blood be less than 500 $\mu\text{mol/L}$. Levels above 500 $\mu\text{mol/L}$ can cause eye problems (that are reversible).

Control - refers to how well the blood levels are controlled by the person with tyrosinemia. "Good control" indicates that the blood tyrosine level is less than 500 $\mu\text{mol/L}$. "Poor control" indicates that the blood tyrosine level is greater than 500 $\mu\text{mol/L}$.

Diagnosis - the identification of a disorder or disease on the basis of its signs and symptoms

Genetics - the study of how our genes influence our growth, development and health

Metabolic disorder - a condition in which an individual cannot break down a substance-often an amino acid-and that substance builds up and causes medical problems. Another metabolic disorder is phenylketonuria (PKU).

Nitisinone - is the medication used to treat tyrosinemia. The brand name is Orfadin[®]. Nitisinone was previously called NTBC.

Phenylalanine - is one of 20 amino acids that make up protein

Protein - long chains of amino acids. Protein is an important nutrient since it provides the amino acids needed for growth and development.

Succinylacetone - in people with untreated tyrosinemia, tyrosine is converted to succinylacetone. Succinylacetone may cause liver and kidney damage and severe neurologic problems. Succinylacetone may cause liver cancer in some children.

Tyrosine - is one of 20 amino acids that make up protein

Tyrosinemia, type 1 - a genetic disorder in which the body cannot completely break down the amino acid tyrosine. It is characterized by higher than normal levels of succinylacetone and tyrosine in the blood which causes damage to the liver and kidneys.

TYROS 1[®] - the registered name of a special milk substitute made for children with tyrosinemia by Mead Johnson, Evansville, IN

Tyrex-1[®] - the registered name of a special milk substitute made for children with tyrosinemia by Ross Products Division, Columbus, OH.

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Revised, January, 2003

