



FAH Deficiency (Tyrosinemia Type 1)

What is it?

This condition is one type of amino acid disorder. People with tyrosinemia 1 have problems breaking down an amino acid called tyrosine from the food they eat. If not treated, the condition causes severe liver disease and other serious health problems.

What causes it?

In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them.

Tyrosinemia 1 occurs when an enzyme, called fumarylacetoacetase (FAH), is either missing or not working properly. When FAH is not working, it cannot break down tyrosine. Tyrosine and other harmful substances then build up in the blood. One of these substances is called succinylacetone. When it builds up in the blood, it causes serious liver and kidney damage. It may also cause episodes of weakness or pain.

If tyrosinemia 1 is not treated, what problems occur?

The symptoms can vary a great deal from person to person. There are two types of tyrosinemia 1. The more common form happens in infants. The less common form is seen in older children and adults.

Tyrosinemia 1 in Infants

Babies usually have symptoms within the first few months of life. Some of the first symptoms may be:

- 1) Diarrhea and bloody stools.
- 2) Vomiting.
- 3) Poor weight gain.
- 4) Extreme sleepiness.
- 5) Irritability.
- 6) Cabbage-like odor to skin or urine.

Liver problems are common. They can lead to:

- 1) Enlarged liver.
- 2) Yellowing of the skin.
- 3) Tendency to bleed and bruise easily.
- 4) Swelling of the legs and abdomen.

Kidney problems also happen and can lead to:

- 1) Rickets, a bone-thinning condition.
- 2) Delays in walking.

Without prompt and careful treatment, babies with severe liver and kidney problems usually die.

Some babies also have episodes that include:

- 1) Pain or weakness, especially in the legs.
- 2) Breathing problems.
- 3) Rapid heartbeat.
- 4) Seizures.
- 5) Coma, sometimes leading to death.

Tyrosinemia 1 in Children (Chronic Form)

Children with the chronic form usually start having symptoms after 2 months of age. Some of the first signs may be trouble gaining weight and episodes of vomiting and diarrhea. Over time, the condition can cause liver, kidney and nerve problems.

Liver

If the condition is not treated, a rare type of liver scarring called nodular cirrhosis can happen. This gets worse over time and can lead to liver failure. If not treated, many children develop liver failure or liver cancer before age 10. Medication, when started early, can prevent liver failure in most children.

Kidney

Serious kidney problems can occur in untreated children. When the kidneys are not working properly, episodes of vomiting, weakness and fever can happen. Rickets, a bone-thinning condition, may happen in children with kidney damage. Medication can prevent kidney problems in most children.

Neurologic Crises

Some children have episodes of weakness, pain or numbness in their arms, legs or other parts of the body. Breathing problems and rapid heartbeat may also happen. Some children have seizures that can lead to coma. Medication can stop episodes of neurologic crisis in most children.

Other

A small number of children have had heart problems. Some have had high blood pressure.

What is the treatment for tyrosinemia 1?

Your baby's doctor will work with a metabolic doctor and dietician to care for your child. Lifelong treatment usually is needed to prevent liver and kidney problems.

Treatment consists of medication and a diet low in tyrosine. The low-tyrosine diet is made up of a special medical formula and carefully chosen foods. You must start the treatment as soon as you know your child has the condition.

The following are treatments often recommended for children with tyrosinemia 1:

Medication

A medication called nitisinone (Orfadin®) is used to prevent liver and kidney damage. It also stops the neurologic crises. The medication also may lessen the risk for liver cancer. Your child should start taking nitisinone as soon as possible. Your doctor will need to write a prescription for this medication.

Nitisinone will increase the level of tyrosine in your child's blood. So, a low-tyrosine diet is a very important part of treatment.

Vitamin D sometimes is used to treat children who have rickets.

Do not take any medication without talking with your doctor.

Medical Formula

The special medical formula gives babies and children the nutrients and protein they need while helping keep their tyrosine levels within a safe range. Your metabolic doctor and dietician will tell you what type of formula is best and how much to use.

Low-Tyrosine Diet

The diet is made up of foods that are very low in tyrosine and another amino acid called phenylalanine. This means your child will need to limit foods such as cow's milk and regular formula. He or she will need to avoid meat, eggs and cheese. Regular flour, dried beans, nuts and peanut butter contain these amino acids also must be limited.

Many vegetables and fruits have only small amounts of phenylalanine and tyrosine and can be eaten regularly in carefully measured amounts.

There are other medical foods such as special flours, pastas and rice that are made especially for people with tyrosinemia 1. Some states offer help with payment, or require private

insurance coverage for formula and other special medical foods.

Your metabolic doctor and dietician will decide on the best food plan for your child. The exact plan will depend on many things, such as your child's age, weight and general health and how well the medication is working. Your dietician will fine-tune your child's diet over time.

Blood, Urine and Other Tests

Your child will have regular blood and urine tests to check:

- 1) Amino acid levels.
- 2) Amount of succinylacetone.
- 3) Nitrosinone level.
- 4) Liver and kidney function.

These tests help your doctor and dietician figure out whether any changes to the medication or diet are needed.

Some experts suggest that children with tyrosinemia 1 have a CT or MRI scan of their liver once a year to check for scarring or cancer.

Liver Transplantation

Before nitrosinone was available, liver transplantation was one of the main treatments for tyrosinemia 1. Now nitrosinone can prevent or reverse many of the liver problems. More time is needed to see if this medication can prevent liver cancer. For most children, nitrosinone will delay, and hopefully prevent, the need for liver transplant.

Liver transplantation is still an option to prevent liver cancer. It also may be considered for children who show signs of liver cancer or liver failure. If you have questions, talk to your metabolic doctor or doctor about the benefits and risks of transplantation.

What happens when tyrosinemia 1 is treated?

When treatment is started early, severe liver, kidney and neurologic symptoms can be

prevented. Children who are treated usually have normal growth and intelligence.

If treatment is not started right away, children may have some liver or kidney damage. Rickets already may be present and need to be treated. Delays in growth and development also may be present. The effects of delayed treatment vary from child to child.

What causes the FAH enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. People with tyrosinemia 1 have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the FAH enzyme does not work properly or is not made at all.

How is tyrosinemia 1 inherited?

The condition is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has a pair of genes that make the FAH enzyme. In children with tyrosinemia 1, neither of these genes works correctly. These children inherit one nonworking gene for the condition from each parent.

Parents of children with tyrosinemia 1 rarely have the condition themselves. Instead, each parent has a single non-working gene for the condition. They are called carriers. Carriers do not have the condition because the other gene of this pair is working correctly.

When both parents are carriers, there is a 25 percent chance in each pregnancy for the child to have tyrosinemia 1. There is a 50 percent chance for the child to be a carrier, just like the parents. And, there is a 25 percent chance for the child to have two working genes.

Can other members of the family have tyrosinemia 1 or be carriers?

Having Tyrosinemia 1

If they are healthy and growing normally, older brothers and sisters of a baby with tyrosinemia 1 are unlikely to be affected. However, finding out whether other children in the family have this condition may be important. Early treatment can prevent serious health problems. Ask your metabolic doctor whether your other children should be tested.

Tyrosinemia 1 Carriers

Brothers and sisters who do not have the condition still have a chance to be carriers like their parents. Except in special cases, carrier testing should be done only in people older than 18.

Each of the parents' brothers and sisters has a 50 percent chance to be a carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with this condition.

When both parents are carriers, newborn screening results are not sufficient to rule out the condition in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening.

Can other family members be tested?

Diagnostic Testing

If there is concern, diagnostic testing can be done on brothers and sisters. Talk to your metabolic doctor if you have questions about testing other family members.

Carrier Testing

If both gene changes have been found in your child, other family members can have DNA testing to see if they are carriers.

If DNA testing is not helpful, other methods of carrier testing may be available. If you have questions about carrier testing, ask your genetic counselor or metabolic doctor.

How many people have tyrosinemia 1?

About one in every 100,000 babies in the United States is born with this condition.

Does tyrosinemia 1 happen more frequently in a certain ethnic group?

This condition occurs in all ethnic groups around the world. It is found more often in people of French-Canadian background, especially in the Saguenay Lac Saint-Jean region of Quebec. About one in 20 French-Canadians in this region are carriers. One in every 1,846 babies in this population is born with the condition.

Does tyrosinemia 1 go by any other names?

Tyrosinemia 1 is sometimes also called:

- 1) Hereditary infantile tyrosinemia.
- 2) Hepatorenal tyrosinemia.
- 3) Fumarylacetoacetase deficiency.
- 4) Fumarylacetoacetate hydrolase deficiency.

Two other forms of this condition – tyrosinemia type II and tyrosinemia type III – have different symptoms and are not discussed in this fact sheet.

Where can I find more information?

About Tyrosinemia: New Parents' Guide
www.depts.washington.edu/tyros/abouttyr.htm

Tyrosinemia Parent Support Group
www.groups.msn.com/tyrosinemia

National Urea Cycle Disorders Foundation
www.nucdf.org

Children Living with Inherited Metabolic Diseases (CLIMB)
www.climb.org.uk

National Coalition for PKU and Allied Disorders
www.pku-allieddisorders.org

Genetic Alliance
www.geneticalliance.org

Children's Special Health Services (CSHS)

State Capitol Judicial Wing
600 E. Boulevard Ave., Department 301
Bismarck, ND 58505-0269
Toll Free: 800.755.2714
701.328.2436
Relay TDD: 701.328.3975
CSHS website: www.ndhealth.gov/CSHS
North Dakota Department of Health website:
www.ndhealth.gov

Family support resources available from CSHS:

- Guidelines of Care Info
- Family Support Packet
- Financial Help Packet
- Insurance Fact Sheet

Family Resources

Family to Family Network
Center for Rural Health
University of North Dakota
School of Medicine and Health Sciences
P.O. Box 9037
Grand Forks, ND 58202-9037
Toll Free: 888.434.7436
701.777.2359
Fax: 701.777.2353
E-mail: NDF2F@medicine.nodak.edu
www.medicine.nodak.edu/crh

Pathfinder Services of ND
Pathfinder Family Center
1600 2nd Ave. SW, Ste. 19
Minot, ND 58701
Toll Free: 800.245.5840
701.837.7500
Relay TDD: 701.837.7501
E-mail: ndpath01@ndak.net
www.pathfinder.minot.com

Family Voices of North Dakota, Inc.
P.O. Box 163
Edgeley, ND 58433
Toll Free: 888.522.9654
701.493.2634
Fax: 701.493.2635
www.geocities.com/ndfv

**This fact sheet has general information. Every child is different and some of these facts may not apply to your child specifically. Certain treatments may be recommended for some children but not others. All children should be followed by a metabolic doctor in addition to their primary-care provider.

Acknowledgement

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Disclaimer

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