



## Newborn Screening ACT Sheet

### Increased Tyrosine Tyrosinemia

**Differential Diagnosis:** Tyrosinemia I (hepatorenal); Tyrosinemia II (oculocutaneous); Tyrosinemia III; transient hypertyrosinemia; liver disease.

**Condition Description:** In the hepatorenal form, tyrosine from ingested protein and phenylalanine metabolism cannot be metabolized by fumarylacetoacetate hydrolase to fumaric acid and acetoacetic acid. The resulting fumarylacetoacetate accumulates and is converted to succinylacetone, the diagnostic metabolite, which is liver toxic, and leads to elevated tyrosine. Tyrosinemias II and III are due to other defects in tyrosine degradation.

#### You Should Take the Following IMMEDIATE Actions

- Contact family to inform them of the newborn screening result.
- Consult with pediatric metabolic specialist. (See attached list.)
- Evaluate the newborn and refer as appropriate.
- Initiate confirmatory/diagnostic tests in consultation with metabolic specialist.
- Initial testing: plasma quantitative amino acids; urine organic acids (including succinylacetone); and liver function tests.
- Repeat newborn screen if the second screen has not been done.
- Provide family with basic information about tyrosinemia.
- Report findings to newborn screening program.

**Diagnostic Evaluation:** Plasma amino acid analysis will show increased tyrosine in all of the tyrosinemias. Urine organic acid analysis will reveal increased succinylacetone in Tyrosinemia I.

**Clinical Considerations:** Tyrosinemia I is usually asymptomatic in the neonate. If untreated, it will cause liver disease and cirrhosis early in infancy. Nitisone (NTBC) treatment will usually prevent these features. Tyrosinemia II is asymptomatic in the neonate, but will cause hyperkeratosis of the skin, corneal ulcers, and in some cases, mental retardation unless treated with a tyrosine restricted diet. Tyrosinemia III may be benign.

#### Additional Information:

##### New England Metabolic Consortium

<http://www.childrenshospital.org/newenglandconsortium/NBS/descriptions/tyro1.html>

<http://www.childrenshospital.org/newenglandconsortium/NBS/descriptions/tyro2.html>

<http://www.childrenshospital.org/newenglandconsortium/NBS/descriptions/tyro3.html>

##### Genetics Home Reference

<http://ghr.nlm.nih.gov/condition=tyrosinemia>

##### STAR G FELSI

<http://www.newbornscreening.info/Parents/aminoacid disorders/Tyrosinemia.html>

<http://www.newbornscreening.info/Pro/aminoacid disorders/Tyrosinemia.html>



## Newborn Screening FACT Sheet

### Tyrosinemia (TYR1)

#### What is TYR1?

TYR1 is an amino acid disorder. People with TYR1 can't break down the amino acid tyrosine from the food they eat. This causes severe liver disease and other health problems if not treated.

#### What Causes TYR1?

Enzymes help start chemical reactions in the body. TYR1 happens when the enzyme fumarylacetoacetase (FAH) is missing or not working. When FAH doesn't work, it can't break down tyrosine. Tyrosine and other harmful things then collect in the blood. One of these is succinylacetone. This causes serious liver and kidney damage. It can also cause periods of weakness or pain.

#### What Symptoms or Problems Occur with TYR1?

*[Symptoms are something out of the ordinary that a parent notices.]*

Babies usually show symptoms in the first few months of life. Some of the first signs are:

- diarrhea and bloody stools
- vomiting
- poor weight gain
- too much sleepiness
- irritable mood
- "cabbage-like" odor to the skin or urine

Liver problems are common. They can cause:

- enlarged liver
- yellow skin
- bleeding and bruising easily
- swollen legs and stomach

Kidney problems also happen and can cause:

- rickets, a bone thinning condition
- delays in walking

Babies with severe liver and kidney problems usually die without quick treatment.

#### What is the Treatment for TYR1?

Doctors use these treatments for children with TYR1:

**1. Medication** – The doctor may prescribe Nitisinone (Orfadin®). This prevents liver and kidney damage. It also stops the weakness and pain. This medicine may lessen the risk of liver cancer. Your child should take Nitisinone right away.

**2. Medical Formula** – The doctor may prescribe a special formula with the right amount of amino acids. He or she will tell you what kind is best and how much to use.

**3. Low-tyrosine diet:** Most children with TYR1 need to limit foods such as cow's milk and regular formula. Your doctor and dietitian will decide on the best food plan for your child. Dietitians know what are the right formulas and foods to eat.

**4. Blood, urine, and other tests** – Regular blood and urine tests will show if your child's diet or medicine needs to be changed.

**5. Liver transplantation** – A liver transplant is one way to prevent liver cancer.

#### Things to Remember

Early treatment can prevent severe symptoms of liver and kidney problems and weakness and pain. Children who are treated early usually have normal growth and intelligence.

If treatment isn't started right away, children may have liver or kidney damage. Rickets might be a problem and need treatment. Delays in growth and development can also happen.