

<b>Disease Name</b>	<b>Tyrosinemia type I</b>
<b>Alternate name(s)</b>	Hereditary infantile tyrosinemia, Hepatorenal tyrosinemia, Fumarylacetoacetase deficiency, Fumarylacetoacetate hydrolase
<b>Acronym</b>	FAH deficiency
<b>Disease Classification</b>	Amino Acid Disorder
<b>Variants</b>	Yes
<b>Variant name</b>	Tyrosinemia I chronic-type, Tyrosinemia II, Tyrosinemia III
<b>Symptom onset</b>	Infancy
<b>Symptoms</b>	Hepatocellular degeneration leading to acute hepatic failure or chronic cirrhosis and hepatocellular carcinoma, renal Fanconi syndrome, peripheral neuropathy, seizures and possible cardiomyopathy.
<b>Natural history without treatment</b>	Chronic liver disease leading to cirrhosis and hepatocellular carcinoma. Renal tubular disease (Fanconi syndrome) with phosphaturia, aminoaciduria and often glycosuria. May lead to clinical rickets. Peripheral neuropathy. Self-injurious behavior, seizures and cardiomyopathy have been observed. Coagulation problems.
<b>Natural history with treatment</b>	Hepatic disease may progress despite dietary treatment. NTBC treatment leads to improvements in kidney, liver and neurologic function, but may not affect incidence of liver cancer.
<b>Treatment</b>	Dietary restriction of phenylalanine and tyrosine. NTBC (2-(2-nitro-4-trifluoromethylbenzoyl)-1, 3-cyclohexanedione) treatment which improves hepatic and renal function. Liver transplantation when indicated to prevent hepatocellular carcinoma. Vitamin D to heal rickets.
<b>Other</b>	Unpleasant odor due to accumulation of methionine. Sometimes described as "cabbage-like" odor.
<b>Physical phenotype</b>	No abnormalities present at birth. May develop widely-spaced incisors, pes planus, epicanthus and microcephaly.
<b>Inheritance</b>	Autosomal recessive
<b>General population incidence</b>	1:100,000
<b>Ethnic differences</b>	Yes
<b>Population</b>	French Canadian (Saguenay-Lac Saint Jean region) 1:20 carrier rate
<b>Ethnic incidence</b>	1:1846
<b>Enzyme location</b>	Liver, kidney, lymphocytes, fibroblasts
<b>Enzyme Function</b>	Metabolizes fumarylacetoacetic acid into fumaric acid and acetoacetic acid
<b>Missing Enzyme</b>	Fumarylacetoacetate hydrolase
<b>Metabolite changes</b>	Increased urinary succinylacetone, increased tyrosine and methionine in serum, increased alpha fetoprotein.
<b>Prenatal testing</b>	Enzymatic assay of amniocytes or CVS cells. Direct DNA testing in amniocytes or CVS cells if mutations known. Succinylacetone in amniotic fluid.
<b>MS/MS Profile</b>	N/A
<b>OMIM Link</b>	<a href="http://www.ncbi.nlm.nih.gov/omim/276700">http://www.ncbi.nlm.nih.gov/omim/276700</a>
<b>Genetests Link</b>	<a href="http://www.genetests.org">www.genetests.org</a>
<b>Support Group</b>	National Urea Cycle Disorders Foundation <a href="http://www.nucdf.org">http://www.nucdf.org</a> National Coalition for PKU and Allied Disorders <a href="http://www.pku-allieddisorders.org/">http://www.pku-allieddisorders.org/</a> Children Living with Inherited Metabolic Diseases <a href="http://www.climb.org.uk/">http://www.climb.org.uk/</a>

## 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.

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**YOU SHOULD TAKE THE FOLLOWING ACTIONS:**

- Contact family to inform them of the newborn screening result.
- Consult with pediatric metabolic specialist.
- Evaluate the newborn and refer as appropriate.
- Initiate confirmatory/diagnostic tests in consultation with metabolic specialist.
- Provide family with basic information about tyrosinemia.
- Report findings to newborn screening program.

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**Diagnostic Evaluation:** Plasma amino acid analysis will show increased tyrosine in all of the tyrosinemias. Urine organic acid analysis may 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. Nitisinone (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:**

[Gene Reviews \(Tyrosinemia I\)](#)  
[Genetics Home Reference](#)

**Referral (local, state, regional and national):**

Testing

[Tyrosinemia I](#)  
[Tyrosinemia II](#)  
[Tyrosinemia III](#)  
[Clinical Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

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