



In this month's newsletter we discuss a case in which elevated levels of Tyrosine were detected. It traces the process we go through to confirm the disorder.

## Case Study:

On July 21, 2008, we reported above normal Tyrosine levels in a newborn baby that was screened routinely. We requested and received a second sample on July 25, 2008. The second sample was Presumptive Positive for Tyrosinemia Type I, II or III or Transient Tyrosinemia of the Newborn. The next step we recommended was to carry out confirmatory testing by urine Organic Acid analysis and plasma Amino Acid analysis. The testing was done by a lab in Hyderabad using HPLC and GC/MS on samples collected on August 2, 2008. The results turned out to be negative for Tyrosinemia Type I, II or III. The probable cause for the elevated levels of Tyrosine was Transient Tyrosinemia of the Newborn, a condition that is not genetic and that is caused by vitamin C deficiency, or immature liver enzymes due to premature birth, or liver dysfunction.

## Tyrosinemia (TYR)

**TYR** is a genetic disorder characterized by elevated blood levels of the amino acid tyrosine, a building block of most proteins. Tyrosinemia is caused by the shortage (deficiency) of one of the enzymes required for the multi-step process that breaks down tyrosine. If untreated, tyrosine and its byproducts build up in tissues and organs, which lead to serious medical problems.

There are three types of Tyrosinemia. Each has distinctive symptoms and is caused by the deficiency of a different enzyme.

**Tyrosinemia (Type I)**, the most severe form of this disorder, is caused by a shortage of the enzyme fumarylacetoacetate hydrolase (FAH). Elevations of plasma tyrosine, often with methionine and perhaps a generalized aminoacidemia are seen in Tyrosinemia Type I. Symptoms usually appear in the first few months of life and include failure to gain weight and grow at the expected rate (failure to thrive), diarrhea, vomiting, yellowing of the skin and whites of the eyes (jaundice), cabbage-like odor, and increased tendency to bleed (particularly nosebleeds). Type I Tyrosinemia can lead to hepatorenal failure, problems affecting the nervous system, and an increased risk of liver cancer. The finding of succinylacetone in urine is pathognomonic for Type I disease

**Tyrosinemia (Type II)** is caused by a deficiency of the enzyme tyrosine aminotransferase (TAT). Patients with Type II usually have an isolated elevation of tyrosine only. This form of the disorder can affect the eyes, skin, and mental development. Symptoms often begin in early childhood and include excessive tearing, abnormal sensitivity to light (photophobia), eye pain

and redness, and painful skin lesions on the palms and soles. About 50 percent of affected individuals have some degree of mental retardation.

**Tyrosinemia (Type III)** is a rare disorder caused by a deficiency of the enzyme 4-hydroxyphenylpyruvate dioxygenase (4HPPD). Characteristic features include mild mental retardation, seizures, and periodic loss of balance and coordination (intermittent ataxia). Patients with Type III have 4-hydroxyphenylpyruvic and 4-hydroxyphenyllactic acids in their urine which can be detected by organic acid analysis.

About 10 percent of newborns have temporarily elevated levels of tyrosine. In these cases, the cause is not genetic but due to **Transient Tyrosinemia of the Newborn**. Normalization of tyrosine level is hastened by dietary supplementation with Vitamin C.

## How do people inherit Tyrosinemia?

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## How common is Tyrosinemia?

Worldwide, Type I Tyrosinemia affects about 1 person in 100,000. Type II Tyrosinemia occurs in less than 1 in 250,000 individuals. Type III Tyrosinemia is very rare; only a few cases have been reported

## Healthcare Professional Resources

1. ACT Sheets

<http://ghr.nlm.nih.gov/condition=tyrosinemia/show/ACTion+Sheets>

2. Gene Reviews

<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=tyrosinemia>

The above information is reproduced from NIH

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

## July 2008 Statistics

- 1 case of MSUD
- 1 case of MMA/PA
- 1 case of VLCAD
- 1 case of a Urea Cycle Disorder (OTC)

## Screening Panels

- **First Step** (Over 50 IEMs for Rs. 3975)
- **First Step MS/MS** (45 IEMs, includes Fatty Acid Oxidation Disorders, Amino Acid Disorders, and Organic Acid Disorder panels for Rs. 3250)
- **First Step Bio** (5 IEMs which include CH, CAH, G6PD, GALT and Cystic Fibrosis for Rs.1250).

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