**Medical Information Sheet**

**TYROSINEMIA**

**What is tyrosinemia?**

Hereditary tyrosinemia is a genetic inborn error of metabolism associated with severe liver disease in infancy. The disease is inherited in an autosomal recessive fashion which means that in order to have the disease, a child must inherit two defective genes, one from each parent. In families where both parents are carriers of the gene for the disease, there is a one in four risk that a child will have tyrosinemia.

About one person in 100,000 is affected with tyrosinemia globally. However, the disease is particularly common in the region of Saguenay-Lac-St-Jean, Quebec where one person in 20 is a carrier of the defective gene, and one person in 1,846 is affected with the actual disease.

**How is tyrosinemia caused?**

Tyrosine is an amino acid which is found in most animal and plant proteins. The metabolism of tyrosine in humans takes place primarily in the liver.

Tyrosinemia is caused by an absence of the enzyme *fumarylacetoacetate hydrolase* (FAH) which is essential in the metabolism of tyrosine. The absence of FAH leads to an accumulation of toxic metabolic products in various body tissues, which in turn results in progressive damage to the liver and kidneys.

**What are the symptoms of tyrosinemia?**

The clinical features of the disease tend to fall into two categories, *acute* and *chronic*.

In the so-called *acute* form of the disease, abnormalities appear in the first month of life. Babies may show poor weight gain, an enlarged liver and spleen, a distended abdomen, swelling of the legs, and an increased tendency to bleeding, particularly nose bleeds. Jaundice may or may not be prominent. Despite vigorous therapy, death from hepatic failure frequently occurs between three and nine months of age unless a liver transplantation is performed.

Some children have a more *chronic* form of tyrosinemia with a gradual onset and less severe clinical features. In these children, enlargement of the liver and spleen are prominent, the abdomen is distended with fluid, weight gain may be poor, and vomiting and diarrhea occur frequently. Affected patients usually develop cirrhosis and its complications. These children also require liver transplantation.
How is tyrosinemia diagnosed?

The diagnosis of tyrosinemia is based on blood and urine tests. In both the acute and chronic forms of the disease, liver function tests are often abnormal. Low serum albumin and clotting factors are also frequently found. Transaminase levels in the blood may be mildly to moderately elevated, and the bilirubin level is increased to a variable extent. Because of the biochemical defect, abnormal products may be measured in the urine which confirm the diagnosis.

Prenatal diagnosis is possible and can be performed by measuring succinylacetone or FAH levels in the amniotic fluid.

In 1992, Dr. Robert Tanguay, a researcher at Laval University, discovered the gene responsible for the production of FAH. This initial discovery was later followed by the identification of a mutation in the FAH gene occurring in 96% of those affected with tyrosinemia in the region of Saguenay-Lac-St-Jean. This important breakthrough has led Dr. Tanguay and his colleagues to develop a molecular test to detect carriers of the mutated gene. Couples at high risk of being carriers are therefore now able to determine their risk of having a child with tyrosinemia.

How is tyrosinemia treated?

It is customary to place affected infants on diets low in phenylalanine, methionine and tyrosine. Given tyrosine is found in protein, meats, dairy products, and other protein-rich foods such as nuts and beans should be avoided. Strict attention to nutrition and adequate vitamin and mineral intake do not cure tyrosinemia, but serve to control the metabolic abnormalities and support normal development and growth.

In addition to dietary modification, treatment with nitisinone (also known as NTBC, an abbreviation of its full chemical name) has been shown to be beneficial. Long-term studies are necessary to determine whether this drug may prevent or only delay liver complications.

At the present time, liver transplantation remains the only effective means of establishing normal enzyme activity and treating the disease once it has reached the more advanced stages.

The Canadian Liver Foundation’s mandate is to reduce the incidence and impact of all liver diseases. If you would like more information about liver health, tyrosinemia and other forms of liver disease, please contact:

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