

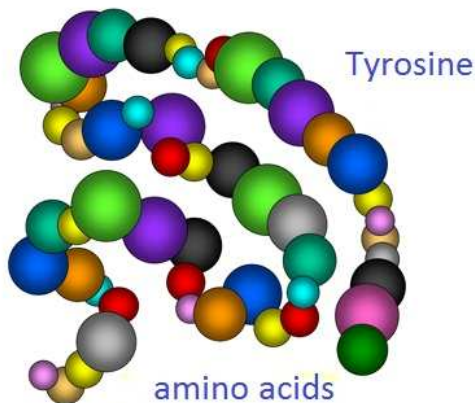
TYPE I TYROSINEMIA

WHAT IS TYPE 1 TYROSINEMIA?

Type 1 tyrosinemia is an **inborn error of tyrosine metabolism** that causes the accumulation of this amino acid in plasma, urine and tissues, and also elevated levels of **potentially toxic products**, particularly **succinylacetone**.

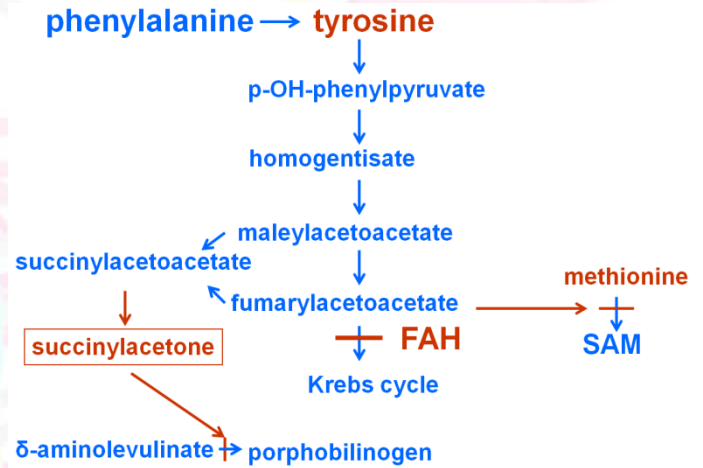
WHAT IS TYROSINE?

Tyrosine is an amino acid found in proteins (long chains of amino acids). It is synthesized from phenylalanine and also formed directly by the degradation of dietary proteins. Tyrosine is normally metabolized through a series of enzymatic reactions and is converted into energy during Krebs cycle.



WHAT HAPPENS IN TYROSINEMIA?

Type 1 tyrosinemia is caused by the deficiency of the enzyme **fumaryl acetoacetate hydrolase (FAH)**. This deficiency causes the accumulation of some amino acids such as tyrosine and methionine and some toxic substances, such as **succinylacetone** and **succinylacetoacetate**, which in turn, inhibit porphyrin metabolism.



WHAT CAUSES FAH DEFICIENCY?

FAH deficiency is caused by mutations (stable, hereditary changes) in the **FAH gene**, which encodes this enzymatic protein. Tyrosinemia is an autosomal recessive disorder.

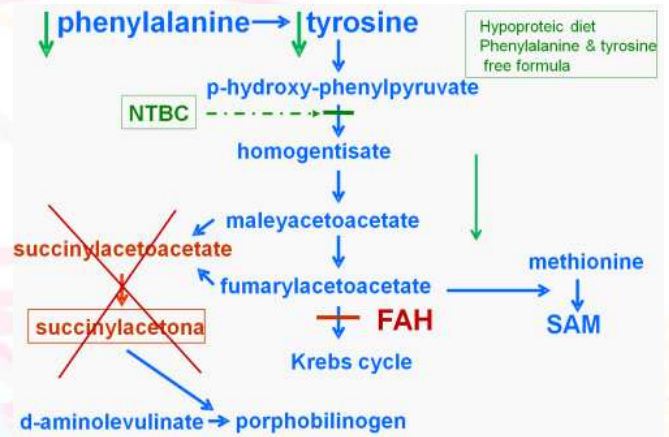
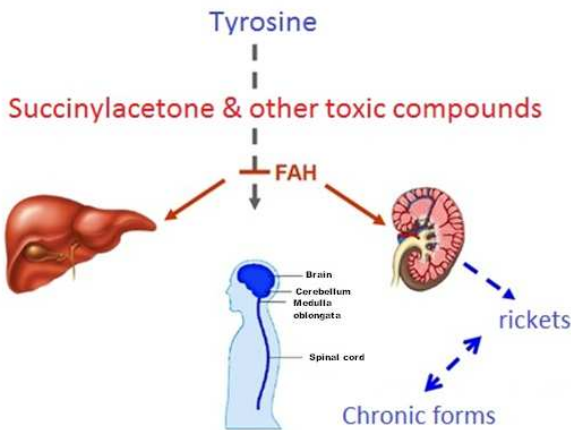
WHAT HAPPENS WHEN AN INFANT IS BORN WITH TYROSINEMIA?

The baby is born without problems as the mother metabolizes the proteins correctly until birth, even though she is a carrier of this wrong genetic information. When the child starts to be fed, milk proteins break and release all the amino acids.

Tyrosine is not degraded properly due to the enzymatic defect and the toxic substances mentioned above **start to accumulate**. As a result of these toxic derivatives, **intoxication of the liver and kidneys of the infant occurs gradually**, leading to clinical symptoms of the disorder in the child

WHICH ARE THE CLINICAL SYMPTOMS OF TYPE 1 TYROSINEMIA?

Type 1 tyrosinemia can have an **early, acute onset**, with a fast deterioration of liver and kidney functions. However, **chronic forms** with kidney dysfunction that may lead to rickets and cirrhosis or even peripheral nervous system, also exist.



HOW IS TYPE 1 TYROSINEMIA DIAGNOSED?

Diagnosis is based on clinical suspicion, on determination of amino acid levels in plasma and urine and on determination of organic acids in urine. The plasma amino acid profile shows elevated levels of tyrosine and methionine, and high excretion of amino-levulinic acid in urine. Organic acid profile shows high succinylacetone levels, which is the key compound for the diagnosis of this disorder. Other less specific but altered biochemical parameters are alpha-fetoprotein, aminotransferases and coagulation factors. These findings must be confirmed by demonstrating the decreased enzyme activity of FAH and/or confirming the mutations in the *FAH gene*.

WHAT CAN BE DONE TO AVOID THE CONSEQUENCES OF TYROSINEMIA?

The diagnosis has to be established as soon as possible and the **specific treatment started** at once. Treatment basically consists of **preventing the accumulation of toxic products which can be done in several ways.**

- a) **First, precursors must be eliminated from the diet, thus avoiding their future accumulation.** This will be achieved, in the first instance, **by restricting the natural proteins of the diet** since all of them contain the precursor amino acids (phenylalanine and tyrosine).

However, **amino acids are essential** for the synthesis of proteins that will make up the body of the baby, therefore proteins are provided by means of a **SPECIAL FORMULA** that does not contain tyrosine and phenylalanine.

- b) In addition, **the formation of toxic products can be avoided with a drug called NTBC that inhibits the tyrosine metabolic pathway** prior to their formation. This will **prevent the liver and kidneys of the infant from accumulating toxic compounds**, enabling them to function properly.

Type 1 tyrosinemia is a hereditary disorder, which if left untreated, can lead to serious consequences. However, if the disorder is rapidly diagnosed and adequately treated, affected children will enjoy a **good quality of life**.

Translation

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