

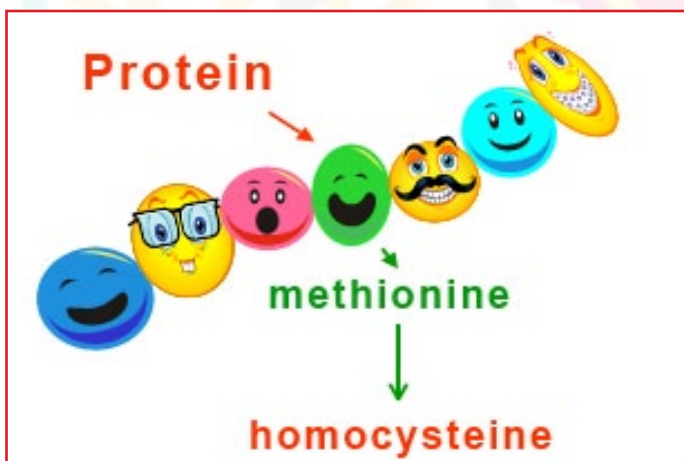
HOMOCYSTINURIA

WHAT IS HOMOCYSTINURIA?

Homocystinuria is a disorder of the metabolism of the homocysteine that causes an accumulation of plasma, urine, and tissues of this amino acid.

WHERE DOES HOMOCYSTEINE COME FROM?

Homocysteine is a sulfured is a non-proteinogenic amino acid (i.e. it doesn't form part of the proteins). It comes from methionine, which is another amino acid that does form part of the proteins.



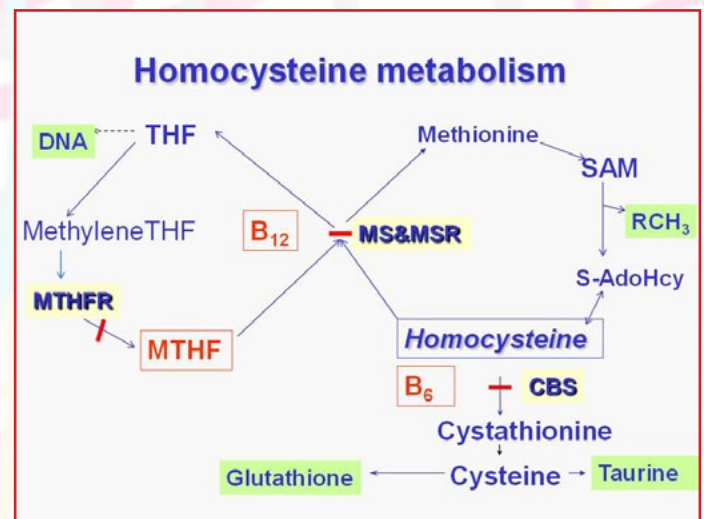
Proteins are formed by a very long chain of amino acids that are liberated when they degrade. The free amino acids can be used to form other proteins, or to generate energy. Each amino acid degrades through a series of chain reactions, forming metabolic pathways. So each amino acid has its own route to form itself and to degrade itself, becoming energy. All these reactions are made thanks to the action of some proteins, enzymes, which facilitate them.

WHAT IS A METABOLIC ERROR?

When there is a metabolic error some of these reactions are not made with the correct effectiveness. When this happens the previous compounds of the reaction accumulate, while the later ones don't synthesize correctly.

WHAT HAPPENS IN HOMOCYSTINURIA?

Homocystinuria is a metabolic error of the homocysteine, which can be caused by the deficiency of different enzymes. The most frequent is the deficiency of cystathionine β -synthase (CBS), also called classical homocystinuria. Because of this, amino acids are accumulated, like homocysteine and methionine, while others are deficient, like the cysteine. This last amino acid is a precursor of other important metabolic substances, like for example, glutathione, which is an important antioxidant and can be deficient in homocystinuria.

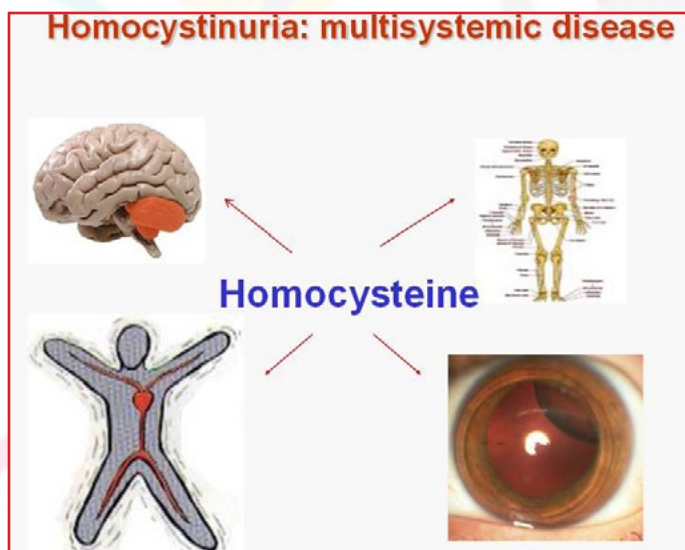


WHY IS THE CLASSICAL HOMOCYSTINURIA PRODUCED?

Each one of the metabolic reactions that create the compounds that form our body is genetically determined (encoded). We all inherit from our parents the correct or altered information that determines if each of the metabolic reactions will take place. The classical homocystinuria occurs due to a deficiency of CBS activity caused by mutations (changes that are stable and inherited) in the gene encoding this enzyme CBS. This deficiency is a genetic disorder of autosomal recessive inheritance. Parents are carriers of mutations in this gene even though they do not suffer the effects of enzyme deficiency. If both parents pass on a mutation to the child, the child will suffer a classical homocystinuria.

WHAT HAPPENS IF A CHILD IS BORN WITH HOMOCYSTINURIA?

The baby is born without problems, because until the time of delivery it's the mother who is responsible for metabolizing protein and she does it well, even though she is the carrier of the wrong information. When the baby starts to feed, the milk proteins degrade and release all the amino acids, including methionine, the precursor of homocysteine. Homocysteine does not degrade well due to the enzymatic defect of CBS and it begins to accumulate, part of it becoming methionine. Homocysteine is a mid to long term toxic amino acid with possible undesired effects on the skeletal system (osteopenia), the ocular system (lens dislocation, myopia), the nervous system (mental retardation, psychiatric disorders, dystonia), and the vascular system (strokes) of the child.



HOW IS THE CLASSICAL HOMOCYSTINURIA DIAGNOSED?

It is diagnosed based on clinical presentation, by the analysis of amino acids in blood and urine, which will show a high concentration of homocysteine and methionine and low concentration of cysteine. The enzymatic study and the mutational analysis of the CBS gene confirm classical homocystinuria and permit genetic counseling.

Translation

American School of Barcelona

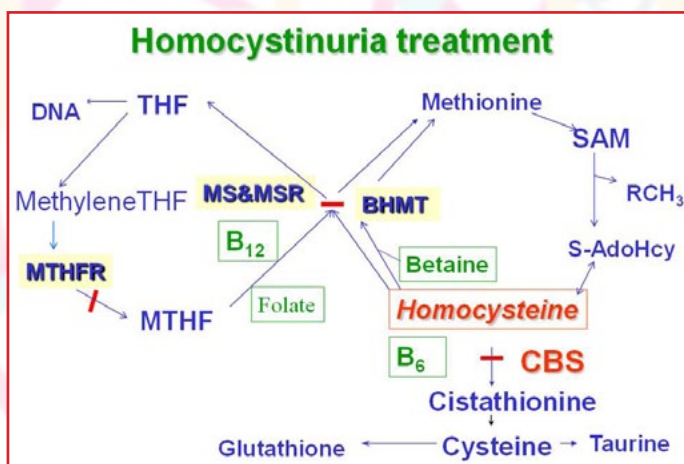
WHAT DO YOU NEED TO DO TO AVOID THE CONSEQUENCES OF HOMOCYSTINURIA?

We must establish a specific treatment. This is based simply on avoiding the accumulation of homocysteine in several ways:

- Vitamin B6, which is the cofactor of CBS, is an essential substance for proper functioning. Some patients respond to this treatment and require no other.
- Adding vitamin B12 and folate to vitamin B6, to ensure that the conversion of homocysteine to methionine (less toxic than homocysteine) is possible.
- Adding betaine to ensure the transformation by other means.
- Eliminate methionine from the diet. This will be achieved by restricting the natural proteins in the diet, because they all contain it.

However, the amino acids are essential for the formation of proteins that will constitute the child's body, so they will be provided with a special formula that contains all other amino acids except methionine.

Homocystinuria is an inherited disease that, if it is untreated, can lead to serious consequences. However the early diagnosis and treatment of the disease may greatly improve the prognosis and quality of life of patients.



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