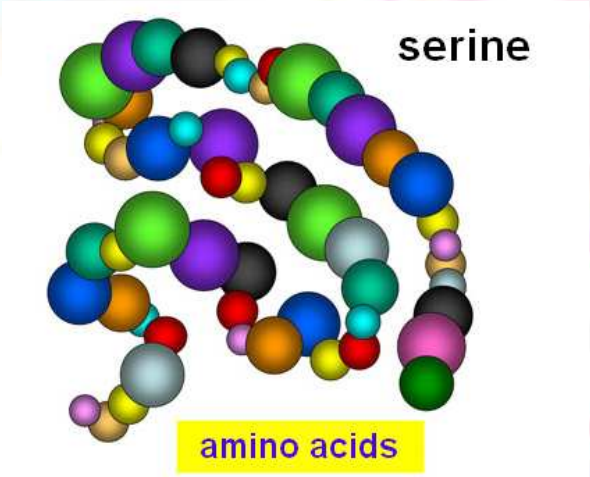
SERINE DEFICIENCY

WHAT IS SERINE DEFICIENCY?

Serine deficiencies are a series of inborn metabolic errors that affect the synthesis of this amino acid. These errors cause a deficiency in the amino acid which mainly affects the nervous system.

WHAT IS SERINE?

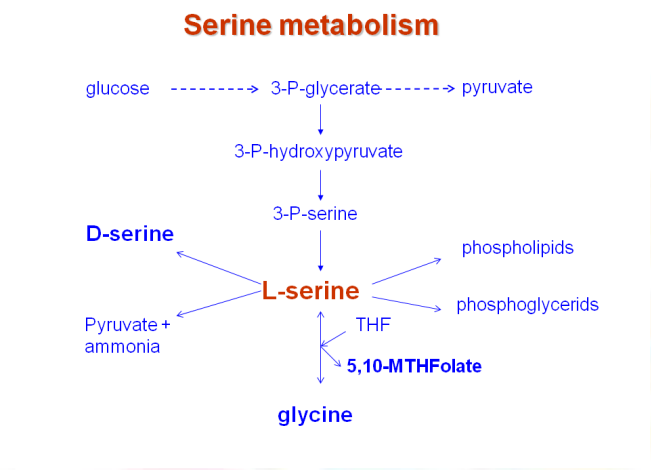


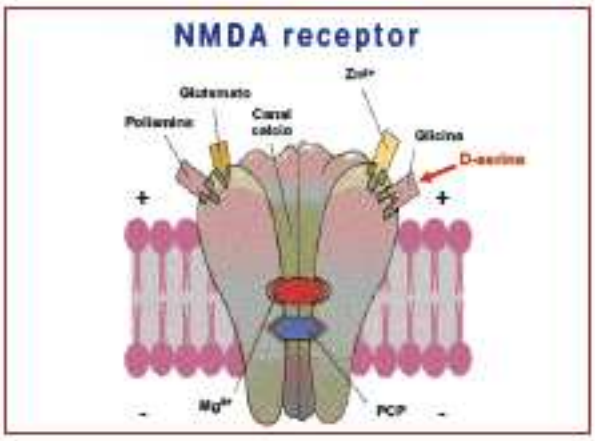
Serine is an amino acid, a simple molecule that is part of proteins. However serine is not essential in the human diet because we can synthesize it from other compounds.

HOW IS SERINE SYNTHESIZED?

Serine is synthesized from 3-phosphopyruvate by means of three enzymatic reactions. Serine can be transformed into the amino acid glycine by means of a reversible reaction in which the folates are metabolized. Serine is the precursor of other amino acids like cystathionine and cysteine and other important compounds like glutathione, purines and pyrimidines. It is essential in the synthesis of phospholipids and phosphoglycerides. These two kinds of compounds are very important for the body metabolism, especially for the brain.

L-Serine is a common form of this amino acid and can become D-serine. D-serine is similar to glycine, in that it is a neuromodulator for the N-methyl-D-aspartate receptor. The N-methyl-D-aspartate (NMDA) is a glutamate receptor that is involved in the development of the nervous system, in brain plasticity and in neurodegeneration. D-Serine is particularly present in the brain during development in prenatal stage.



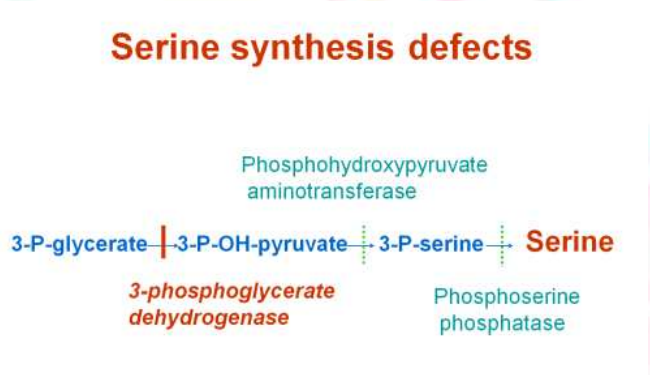


WHAT IS A METABOLIC ERROR?

When there is an alteration (error) in the metabolism (set of enzymatic reactions that allow us to live), some metabolic processes do not function effectively, resulting in the deficiency of some compounds that haven't been formed correctly, and are essential for our body. This would be the case of serine. These alterations have pathological consequences.

WHAT HAPPENS IN SERINE DEFICIENCY?

Serine deficiency could happen due to a defect in any of the three enzymes involved in its synthesis. The most frequent defect is 3-phosphoglycerate dehydrogenase (PHGDH) deficiency that is also the most serious.



WHY DOES A PHGDH DEFICIENCY OCCUR?

Each of the metabolic reactions that lead to the compounds that form our body is genetically determined (encoded). We all inherit from our parents the correct or altered information that determines how each of these metabolic processes work. The deficiency in the activity of the PHGDH enzyme occurs due to a mutation (stable and hereditary changes) in the PHGDH gene that codify for this enzyme. This deficiency is a genetic disorder of autosomic recessive inheritance. This means that the parents are carriers of PHGDH gene mutations but do not suffer the consequences of the enzyme deficiency. If both of the parents transmit the mutation to their child, he/she will suffer a serine deficiency.

WHAT HAPPENS TO A CHILD BORN WITH SERINE DEFICIENCY?

Children with serine deficiency display neurological symptoms even before they are born because L-Serine, D-serine, Glycine and folate metabolism are very important for the development and the proper function of the central nervous system. An example of this is congenital microcephaly. The delay in the psychomotor development can be displayed in the first few months of life, followed by refractory seizures, cataracts, spastic tetraparesis and nystagmus in some patients.

HOW IS SERINE DEFICIENCY DIAGNOSED?

The diagnosis is based on the analysis of amino acids in the plasma and cerebrospinal fluid of the patient to detect serine deficiency and in some cases also glycine deficiency. The enzymatic study allows for a differential diagnosis between the three synthesizing defects. The genetic study confirms the defect and allows for genetic counseling and prenatal diagnosis.

WHAT CAN BE DONE TO AVOID THE CONSEQUENCES OF SERINE DEFICIENCY?

It is essential to treat the patient as soon as possible, even prenatally in families with previous cases of serine deficiency. The treatment of the defects of serine synthesis is based in the administration of L-serine. L-serine corrects not only the serine deficiency but also the glycine and folate deficiencies. Patients that show a low concentration of plasma glycine can be treated with glycine and serine. Supplementing with serine is very effective in the treatment of epileptic seizures.

Serine deficiency is a disease that if not treated con lead to serious consequences. However, if it is diagnosed and treated as soon as possible these consequences can be avoided or minimized, improving the quality of life of these patients.

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