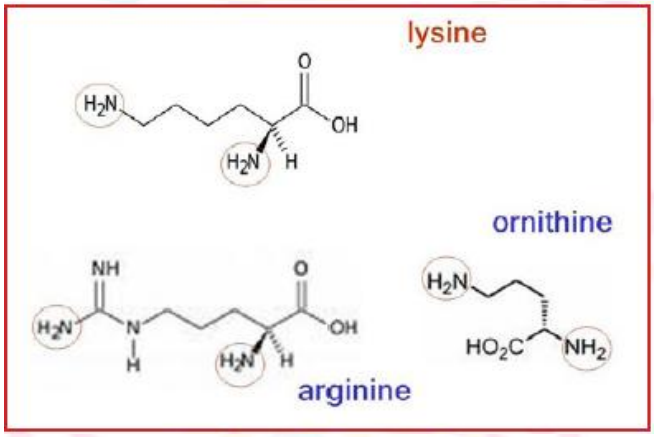
LYSINURIC PROTEIN INTOLERANCE

WHAT IS LYSINURIC PROTEIN INTOLERANCE (LPI)?

LPI is an **inborn error of dibasic amino acid (AA+) transport** caused by a defect of the intestinal and renal transporter of these amino acids. As consequence, a **poor intestinal absorption together with increased renal elimination of dibasic amino acids is observed.**

WHAT ARE DIBASIC AMINO ACIDS (AA+)?

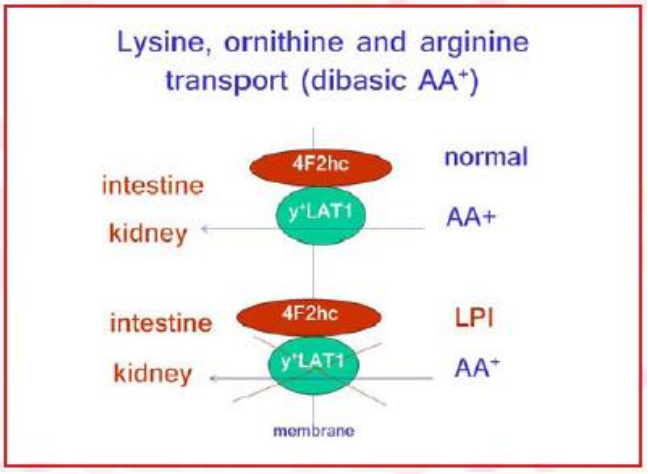
AAs+ (**lysine, ornithine and arginine**) are amino acids that contain two amino groups and one acid group in their structure.



Lysine is an essential amino acid which is not synthesized in the body and therefore must be obtained from dietary proteins. **Ornithine and arginine** are urea cycle intermediary amino acids. Lysine and arginine are proteinogenic amino acids (they are a part of all proteins). All three share the same transport system through the plasma membrane of the small bowel wall and renal epithelial cells.

WHAT HAPPENS IN LPI?

The AA+ transporter is composed of two different proteins, one of which (yLAT 1) can be totally or partially inactivated if its coding gene (***SLC7A7***) is mutated (mutations are stable and hereditary changes)). This causes a "transport error" which produces low intestinal absorption of AA+ and increased renal excretion of these amino acids.



WHY DO WE SAY THAT THIS ERROR IS CONGENITAL?

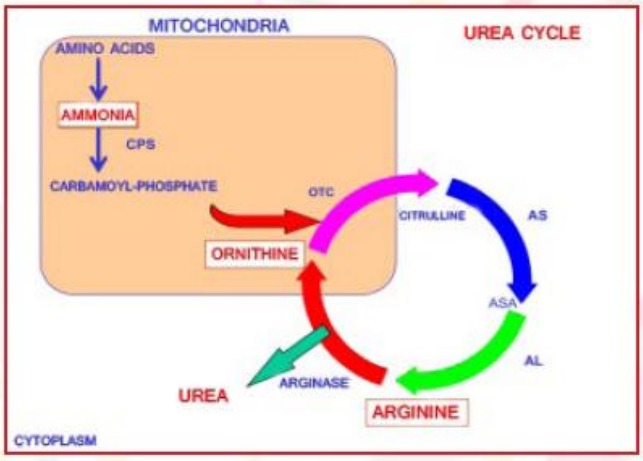
This error is congenital because sufferers of this condition are born with it. It is a hereditary error. Every metabolic process that plays a role in the formation and correct functioning of our organism is genetically determined (coded).

All of us inherit from our parents the correct or altered information which determines the functioning of each of these metabolic processes, in this case, the dibasic amino acid transport. If we inherit incorrect information or partially altered information, that particular metabolic process will function incorrectly leading to a possible hereditary metabolic disorder.

WHAT ARE THE CONSEQUENCES OF A DEFECT IN THE AA+ TRANSPORT SYSTEM?

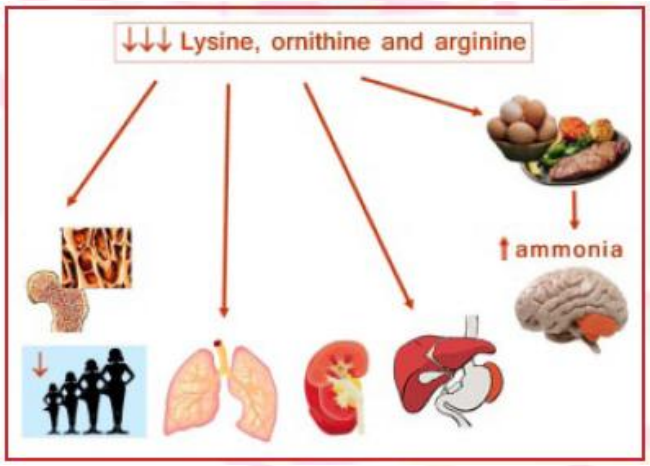
Lysine malabsorption or its loss in large amounts through the kidney (lysinuria) causes a defect of this essential amino acid for **protein synthesis and collagen metabolism**. Also, ornithine and arginine malabsorption causes **interference in the urea cycle** resulting in hyperammonemia with protein intolerance. Therefore, the name of this condition

(lysinuric protein intolerance (LPI)) comes from the above mentioned mechanisms.



WHAT HAPPENS WHEN A CHILD IS BORN WITH LPI?

The infant appears normal at birth and remains asymptomatic during lactation. When the infant starts a diet with a higher protein deficiency of ornithine and arginine occurs and the urea cycle gets affected. Ammonium (which is a by-product of protein metabolism), accumulates. The **hyperammonemia** manifests as vomiting, diarrhea and rejection of protein-rich foods.



Gradually, **lysine deficiency** effects become more evident (growth retardation, osteoporosis). Hepatosplenomegaly, muscular hypotonia, and hair alterations may also appear. Possible severe complications such as chronic respiratory insufficiency which may lead to pulmonary alveolar proteinosis may occur in untreated patients. The immune system may also be affected and glomerulonephritis and multisystem involvement may occur.

HOW IS LPI DIAGNOSED?

Plasma and urinary amino acid analysis will show an anomalous profile with hypoaminoacidemia which exclusively affects the dibasic AAs, with elevated excretion of these amino acids, particularly lysine, in the urine. There is also an increase in the excretion of orotic acid. The mutational study of the ***SLC7A7*** gene which codes the transport protein of AA+ confirms the diagnosis.

WHAT CAN BE DONE TO AVOID THE CONSEQUENCES OF LPI?

Treatment must be started. The treatment will be based on:

1) Avoiding hyperammonemia through a low protein diet. Supplements with citrulline will normalize the urea cycle activity as citrulline is a precursor of the ornithine and arginine amino acids.
2) Avoiding osteoporosis through the administration of calcium, vitamin D and other pharmacological agents.
3) Supplementation with lysine has been suggested in an attempt to correct the low concentration of this amino acid, but with uncertain results.

LPI is a hereditary disorder which, if untreated, can have serious consequences. However, early diagnosis and treatment improve prognosis and the quality of life of affected children.

Translation
American School of Barcelona

Passeig Sant Joan de Déu, 2
08950 Esplugues de Llobregat
Barcelona, Spain
Tel: +34 93 203 39 59
www.hsjdbcn.org / www.guiametabolica.org