Lysinuric protein intolerance

Lysinuric protein intolerance is a disorder caused by the body's inability to digest and use certain protein building blocks (amino acids), namely lysine, arginine, and ornithine. Because the body cannot effectively break down these amino acids, which are found in many protein-rich foods, nausea and vomiting are typically experienced after ingesting protein.

People with lysinuric protein intolerance have features associated with protein intolerance, including an enlarged liver and spleen (hepatosplenomegaly), short stature, muscle weakness, impaired immune function, and progressively brittle bones that are prone to fracture (osteoporosis). A lung disorder called pulmonary alveolar proteinosis may also develop. This disorder is characterized by protein deposits in the lungs, which interfere with lung function and can be life-threatening. An accumulation of amino acids in the kidneys can cause end-stage renal disease (ESRD) in which the kidneys become unable to filter fluids and waste products from the body effectively. A lack of certain amino acids can cause elevated levels of ammonia in the blood. If ammonia levels are too high for too long, they can cause coma and intellectual disability.

The signs and symptoms of lysinuric protein intolerance typically appear after infants are weaned and receive greater amounts of protein from solid foods.

Frequency

Lysinuric protein intolerance is estimated to occur in 1 in 60,000 newborns in Finland and 1 in 57,000 newborns in Japan. Outside these populations this condition occurs less frequently, but the exact incidence is unknown.

Causes

Mutations in the \( SLC7A7 \) gene cause lysinuric protein intolerance. The \( SLC7A7 \) gene provides instructions for producing a protein called \( y^+L \) amino acid transporter 1 (\( y^+LAT-1 \)), which is involved in transporting lysine, arginine, and ornithine between cells in the body. The transportation of amino acids from the small intestines and kidneys to the rest of the body is necessary for the body to be able to use proteins. Mutations in the \( y^+LAT-1 \) protein disrupt the transportation of amino acids, leading to a shortage of lysine, arginine, and ornithine in the body and an abnormally large amount of these amino acids in urine.

A shortage of lysine, arginine, and ornithine disrupts many vital functions. Arginine and ornithine are involved in a cellular process called the urea cycle, which processes excess nitrogen (in the form of ammonia) that is generated when protein is used by the body. The lack of arginine and ornithine in the urea cycle causes elevated levels of ammonia in the blood. Lysine is particularly abundant in collagen molecules that give
structure and strength to connective tissues such as skin, tendons, and ligaments. A deficiency of lysine contributes to the short stature and osteoporosis seen in people with lysinuric protein intolerance. Other features of lysinuric protein intolerance are thought to result from abnormal protein transport (such as protein deposits in the lungs) or a lack of protein that can be used by the body (protein malnutrition).

Inheritance Pattern
This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition
• Congenital lysinuria
• Hyperdibasic aminoaciduria
• LPI
• LPI - Lysinuric protein intolerance

Diagnosis & Management
Genetic Testing Information
• What is genetic testing? https://primer/testing/genetictesting

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22lysinuric+protein+intolerance%22+OR+%22amino+acid+transport+disorders%2C+inborn%22

Other Diagnosis and Management Resources
• MedlinePlus Encyclopedia: Malabsorption https://medlineplus.gov/ency/article/000299.htm
Additional Information & Resources

Health Information from MedlinePlus
- Encyclopedia: Aminoaciduria
  https://medlineplus.gov/ency/article/003366.htm
- Encyclopedia: Malabsorption
  https://medlineplus.gov/ency/article/000299.htm
- Health Topic: Amino Acid Metabolism Disorders
  https://medlineplus.gov/aminoacidmetabolismdisorders.html
- Health Topic: Malabsorption Syndromes
  https://medlineplus.gov/malabsorptionsyndromes.html

Genetic and Rare Diseases Information Center
- Lysinuric protein intolerance

Educational Resources
- MalaCards: lysinuric protein intolerance
  https://www.malacards.org/card/lysinuric_protein_intolerance
- Orphanet: Lysinuric protein intolerance
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=470

Patient Support and Advocacy Resources
- Metabolic Support UK
  https://www.metabolicsupportuk.org/
- National Urea Cyle Disorders Foundation
  http://www.nucdf.org/

Clinical Information from GeneReviews
- Lysinuric Protein Intolerance
  https://www.ncbi.nlm.nih.gov/books/NBK1361

Scientific Articles on PubMed
- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28lysinuric+protein+intolerance+%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
- LYSINURIC PROTEIN INTOLERANCE
  http://omim.org/entry/222700
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17475666

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18200002

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15050971

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17764084

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15776427

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