# Histidinemia

## Description

Histidinemia is an inherited condition characterized by elevated levels of histidine in blood, urine, and the fluid that surrounds the brain and spinal cord (cerebrospinal fluid). Histidine is an amino acid that acts as a building block for many different proteins.

In most cases, histidinemia does not cause health problems. Most people with elevated histidine levels are unaware that they have this condition. Rarely, people with histidinemia have intellectual disabilities, learning disabilities, or behavioral problems. Having a medical complication during or soon after birth might increase the risk of developmental problems in people with histidinemia.

## Frequency

Since many people who have histidinemia do not have signs and symptoms, it is hard to know exactly how many people have the condition. The condition appears to be more common among people of Japanese descent and among the French Canadian population in Quebec, Canada.

## Causes

Histidinemia is caused by variants (also called mutations) in the *HAL* gene, which provides instructions for making an enzyme called histidase. Histidase breaks down histidine that the body gets from food. Histidase is active (expressed) primarily in the liver and the skin.

*HAL* gene variants impair the enzyme's ability to break down histidine, which causes histidine to build up in the blood, urine, and cerebrospinal fluid.

Learn more about the gene associated with Histidinemia

- HAL

## Inheritance

This condition is typically inherited in an autosomal recessive pattern, which means both copies of the gene in each cell must have a variant to cause the disorder. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene.

## Other Names for This Condition

- HAL deficiency
- HIS deficiency
- Histidase deficiency
- Histidine ammonia-lyase deficiency
- Histidinuria
- Hyperhistidinemia

## Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Histidinemia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0220992/)

Genetic and Rare Diseases Information Center

- Histidinemia (https://rarediseases.info.nih.gov/diseases/6661/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- HISTIDINEMIA (https://omim.org/entry/235800)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28histidinemia%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

## References


- Brosco JP, Sanders LM, Dharia R, Guez G, Feudtner C. The lure of treatment: expanded newborn screening and the curious case of histidinemia. Pediatrics. 2010Mar;125(3):417-9. doi: 10.1542/peds.2009-2060. Epub 2010 Feb 15. No abstractavailable. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/20156889)
- Brosnan ME, Brosnan JT. Histidine Metabolism and Function. J Nutr. 2020 Oct1; 150(Suppl 1):2570S-2575S. doi: 10.1093/jn/nxaa079. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/33000155)
- Ishikawa M. Developmental disorders in histidinemia--follow-up study oflanguage development in histidinemia. Acta Paediatr Jpn. 1987 Apr;29(2):224-8.doi: 10.1111/j.1442-200x.1987.tb00037.x. No abstract available. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/2472732)
- Kawai Y, Moriyama A, Asai K, Coleman-Campbell CM, Sumi S, Morishita H, SuchiM. Molecular characterization of histidinemia: identification of four missensemutations in the histidase gene. Hum Genet. 2005 Apr;116(5):340-6. doi: 10.1007/s00439-004-1232-5. Epub 2005 Jan 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15806399)
- Kessler AT, Raja A. Biochemistry, Histidine. 2023 Jul 30. In: StatPearls[Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Availablefrom http://www.ncbi.nlm.nih.gov/books/NBK538201/ Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/30855789)
- Lam WK, Cleary MA, Wraith JE, Walter JH. Histidinaemia: a benign metabolicdisorder. Arch Dis Child. 1996 Apr;74(4):343-6. doi: 10.1136/adc.74.4.343. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/8669938)
- Levy HL, Shih VE, Madigan PM. Routine newborn screening for histidinemia. Clinical and biochemical results. N Engl J Med. 1974 Dec 5;291(23):1214-9. doi:10.1056/NEJM197412052912303. No abstract available. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/4421298)
- Taylor RG, Levy HL, McInnes RR. Histidase and histidinemia. Clinical andmolecular considerations. Mol Biol Med. 1991 Feb;8(1):101-16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/1943682)
- Virmani K, Widhalm K. Histidinemia: a biochemical variant or a disease? J AmColl Nutr. 1993 Apr;12(2):115-24. doi: 10.1080/07315724.1993.10718291. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/8463510)


**Last updated June 3, 2024**