transcobalamin deficiency

Transcobalamin deficiency is a disorder that impairs the transport of cobalamin (also known as vitamin B12) within the body. Cobalamin is obtained from the diet; this vitamin is found in animal products such as meat, eggs, and shellfish. An inability to transport cobalamin within the body results in cells that lack cobalamin, which they need for many functions including cell growth and division (proliferation) and DNA production. The absence of cobalamin leads to impaired growth, a shortage of blood cells, and many other signs and symptoms that usually become apparent within the first weeks or months of life.

The first signs of transcobalamin deficiency are typically a failure to gain weight and grow at the expected rate (failure to thrive), vomiting, diarrhea, and open sores (ulcers) on the mucous membranes such as the lining inside the mouth. Neurological function is impaired in affected individuals, and they can experience progressive stiffness and weakness in their legs (paraparesis), muscle twitches (myoclonus), or intellectual disability.

People with transcobalamin deficiency often develop a blood disorder called megaloblastic anemia. Megaloblastic anemia results in a shortage of red blood cells, and the remaining red blood cells are abnormally large. Individuals with transcobalamin deficiency may also have a shortage of white blood cells (neutropenia), which can lead to reduced immune system function. Decreased cellular cobalamin can lead to a buildup of certain compounds in the body, resulting in metabolic conditions known as methylmalonic aciduria or homocystinuria.

Frequency

The prevalence of transcobalamin deficiency is unknown. At least 45 affected individuals have been described in the medical literature.

Genetic Changes

Mutations in the *TCN2* gene cause transcobalamin deficiency. The *TCN2* gene provides instructions for making a protein called transcobalamin. This protein attaches (binds) to cobalamin and transports the vitamin to cells throughout the body. Within cells, cobalamin helps certain enzymes carry out chemical reactions. Cobalamin plays a role in the processes that produce the building blocks of DNA (nucleotides) and break down various compounds such as fatty acids; these processes are needed for cell proliferation and the production of cellular energy.

Most *TCN2* gene mutations that cause transcobalamin deficiency lead to a complete or near-complete lack (deficiency) of transcobalamin. Other *TCN2* gene mutations result in

a transcobalamin protein that cannot transport cobalamin to cells. The resulting lack of cobalamin within cells interferes with the functioning of certain enzymes, which impacts many cell activities. As a result, a wide range of signs and symptoms can develop including impaired growth, blood cell shortages, and neurological problems.

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

- TC deficiency
- TC II deficiency
- TCN2 deficiency
- transcobalamin II deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Transcobalamin II deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0342701/

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Vitamin B12 Level
  https://medlineplus.gov/ency/article/003705.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Anemia--B12 Deficiency
  https://medlineplus.gov/ency/article/000574.htm
- Encyclopedia: Vitamin B12 Level
  https://medlineplus.gov/ency/article/003705.htm
- Health Topic: B Vitamins
  https://medlineplus.gov/bvitamins.html

Genetic and Rare Diseases Information Center

- Transcobalamin 1 deficiency
  https://rarediseases.info.nih.gov/diseases/5239/transcobalamin-1-deficiency

Additional NIH Resources

- National Heart, Lung, and Blood Institute: What is Anemia?
  https://www.nhlbi.nih.gov/health/health-topics/topics/anemia/
- National Institutes of Health: Office of Dietary Supplements: Vitamin B12
  https://ods.od.nih.gov/factsheets/VitaminB12-Consumer/

Educational Resources

- Centers for Disease Control and Prevention: Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Children's Hospital Boston: Megaloblastic Pernicious Anemia
  http://www.childrenshospital.org/conditions-and-treatments/conditions/megaloblastic-pernicious-anemia
- Children's Hospital Boston: White Blood Cell Disorders
  http://www.childrenshospital.org/conditions-and-treatments/conditions/white-blood-cell-disorders
- CLIMB: Transcobalamin II Deficiency Info Sheet
  http://www.climb.org.uk/IMD/Tango/TranscobalaminIIDeficiency.pdf
- Disease InfoSearch: Transcobalamin II deficiency
  http://www.diseaseinfosearch.org/Transcobalamin+II+deficiency/9416
- MalaCards: transcobalamin ii deficiency
  http://www.malacards.org/card/transcobalamin_ii_deficiency
- Merck Manual Consumer Version: Failure to Thrive
  http://www.merckmanuals.com/home/children-s-health-issues/miscellaneous-disorders-in-infants-and-young-children/failure-to-thrive

- Merck Manual Consumer Version: Vitamin Deficiency Anemia
  http://www.merckmanuals.com/home/blood-disorders/anemia/vitamin-deficiency-anemia
- Merck Manual Professional Version: Vitamin B12
  http://www.merckmanuals.com/professional/nutritional-disorders/vitamin-deficiency,-dependency,-and-toxicity/vitamin-b-12
- Orphanet: Transcobalamin deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=859
- Seattle Children's Hospital: Anemia
  http://www.seattlechildrens.org/kids-health/parents/diseases-and-conditions/heart-and-blood-vessels/anemia/
- Seattle Children's Hospital: Neutropenia
  http://www.seattlechildrens.org/medical-conditions/heart-blood-conditions/neutropenia/
- Washington University, St. Louis: Neuromuscular Disease Center: Vitamin B12 (Cobalamin) Deficiency
  http://neuromuscular.wustl.edu/nother/vitamin.htm#B12

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  http://aaidd.org/
- CLIMB: Children Living with Inherited Metabolic Diseases (UK)
  http://www.climb.org.uk/
- Immune Deficiency Foundation
  http://primaryimmune.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28transcobalamin+II+deficiency%5BTIAB%5D%29+OR+%28transcobalamin+deficiency%5BTIAB%5D%29+OR+%28TCII+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- TRANSCOBALAMIN II DEFICIENCY
  http://omim.org/entry/275350

Sources for This Summary

- Häberle J, Pauli S, Berning C, Koch HG, Linnebank M. TC II deficiency: avoidance of false-negative molecular genetics by RNA-based investigations. J Hum Genet. 2009 Jun;54(6):331-4. doi: 10.1038/jhg.2009.34. Epub 2009 Apr 17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19373259
- Nissen PH, Nordwall M, Hoffmann-Lücke E, Sorensen BS, Nexo E. Transcobalamin deficiency caused by compound heterozygosity for two novel mutations in the TCN2 gene: a study of two affected siblings, their brother, and their parents. J Inherit Metab Dis. 2010 Dec;33 Suppl 3: S269-74. doi: 10.1007/s10545-010-9145-z. Epub 2010 Jul 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20607612
- Prasad C, Rosenblatt DS, Corley K, Cairney AE, Rupar CA. Transcobalamin (TC) deficiency--potential cause of bone marrow failure in childhood. J Inherit Metab Dis. 2008 Dec;31 Suppl 2: S287-92. doi: 10.1007/s10545-008-0864-3. Epub 2008 Oct 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18956254
- Ratschmann R, Minkov M, Kis A, Hung C, Rupar T, Mühl A, Fowler B, Nexo E, Bodamer OA. Transcobalamin II deficiency at birth. Mol Genet Metab. 2009 Nov;98(3):285-8. doi: 10.1016/j.ymgme.2009.06.003. Epub 2009 Jun 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19581117
- Unal S, Tezol O, Oztas Y. A novel mutation of the transcobalamin II gene in an infant presenting with hemophagocytic lymphohistiocytosis. Int J Hematol. 2014;99(5):659-62. doi: 10.1007/s12185-014-1545-7. Epub 2014 Feb 22.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24563082

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