

Childhood myocerebrohepatopathy spectrum

Description

Childhood myocerebrohepatopathy spectrum, commonly called MCHS, is part of a group of conditions called the *POLG*-related disorders. The conditions in this group feature a range of similar signs and symptoms involving muscle-, nerve-, and brain-related functions. MCHS typically becomes apparent in children from a few months to 3 years old. People with this condition usually have problems with their muscles (myo-), brain (cerebro-), and liver (hepato-).

Common signs and symptoms of MCHS include muscle weakness (myopathy), developmental delay or a deterioration of intellectual function, and liver disease. Another possible sign of this condition is a toxic buildup of lactic acid in the body (lactic acidosis). Often, affected children are unable to gain weight and grow at the expected rate (failure to thrive).

Additional signs and symptoms of MCHS can include a form of kidney disease called renal tubular acidosis, inflammation of the pancreas (pancreatitis), recurrent episodes of nausea and vomiting (cyclic vomiting), or hearing loss.

Frequency

The prevalence of childhood myocerebrohepatopathy spectrum is unknown.

Causes

MCHS is caused by mutations in the *POLG* gene. This gene provides instructions for making one part, the alpha subunit, of a protein called polymerase gamma (pol γ). Pol γ functions in mitochondria, which are structures within cells that use oxygen to convert the energy from food into a form cells can use. Mitochondria each contain a small amount of DNA, known as mitochondrial DNA (mtDNA), which is essential for the normal function of these structures. Pol γ "reads" sequences of mtDNA and uses them as templates to produce new copies of mtDNA in a process called DNA replication.

Most *POLG* gene mutations change single protein building blocks (amino acids) in the alpha subunit of pol γ . These changes result in a mutated pol γ that has a reduced ability to replicate DNA. Although the mechanism is unknown, mutations in the *POLG* gene often result in fewer copies of mtDNA (mtDNA depletion), particularly in muscle, brain, or liver cells. MtDNA depletion causes a decrease in cellular energy, which could

account for the signs and symptoms of MCHS.

Learn more about the gene associated with Childhood myocerebrohepatopathy spectrum

POLG

Inheritance

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

• MCHS

Additional Information & Resources

Genetic Testing Information

 Genetic Testing Registry: Progressive sclerosing poliodystrophy (https://www.ncbi.n lm.nih.gov/gtr/conditions/C0205710/)

Patient Support and Advocacy Resources

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

Scientific Articles on PubMed

 PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28POLG%5BTIAB%5D%2 9+AND+%28mtDNA+depletion%5BTIAB%5D%29%29+AND+english%5Bla%5D+A ND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

 Cohen BH, Chinnery PF, Copeland WC. POLG-Related Disorders. 2010 Mar16 [updated 2024 Feb 29]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, WallaceSE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet].Seattle (WA): University of Washington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih. gov/books/NBK26471/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/203017 91)

- Milone M, Massie R. Polymerase gamma 1 mutations: clinical correlations. Neurologist. 2010 Mar;16(2):84-91. doi: 10.1097/NRL.0b013e3181c78a89. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20220442)
- Moraes CT, Shanske S, Tritschler HJ, Aprille JR, Andreetta F, Bonilla E, SchonEA, DiMauro S. mtDNA depletion with variable tissue expression: a novel geneticabnormality in mitochondrial diseases. Am J Hum Genet. 1991 Mar;48(3):492-501. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/1998336) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1682992/)
- Rocher C, Taanman JW, Pierron D, Faustin B, Benard G, Rossignol R, Malgat M, Pedespan L, Letellier T. Influence of mitochondrial DNA level on cellular energymetabolism: implications for mitochondrial diseases. J Bioenerg Biomembr. 2008Apr;40(2):59-67. doi: 10.1007/s10863-008-9130-5. Epub 2008 Apr 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18415670)
- Stumpf JD, Copeland WC. Mitochondrial DNA replication and disease: insightsfrom DNA polymerase gamma mutations. Cell Mol Life Sci. 2011 Jan;68(2):219-33. doi:10. 1007/s00018-010-0530-4. Epub 2010 Oct 8. Citation on PubMed (https://pubmed.nc bi.nlm.nih.gov/20927567) or Free article on PubMed Central (https://www.ncbi.nlm.ni h.gov/pmc/articles/PMC3046768/)

Last updated June 1, 2011