



## Alternating hemiplegia of childhood

Alternating hemiplegia of childhood is a neurological condition characterized by recurrent episodes of temporary paralysis, often affecting one side of the body (hemiplegia). During some episodes, the paralysis alternates from one side of the body to the other or affects both sides at the same time. These episodes begin in infancy or early childhood, usually before 18 months of age, and the paralysis lasts from minutes to days.

In addition to paralysis, affected individuals can have sudden attacks of uncontrollable muscle activity; these can cause involuntary limb movements (choreoathetosis), muscle tensing (dystonia), movement of the eyes (nystagmus), or shortness of breath (dyspnea). People with alternating hemiplegia of childhood may also experience sudden redness and warmth (flushing) or unusual paleness (pallor) of the skin. These attacks can occur during or separately from episodes of hemiplegia.

The episodes of hemiplegia or uncontrolled movements can be triggered by certain factors, such as stress, extreme tiredness, cold temperatures, or bathing, although the trigger is not always known. A characteristic feature of alternating hemiplegia of childhood is that all symptoms disappear while the affected person is sleeping but can reappear shortly after awakening. The number and length of the episodes initially worsen throughout childhood but then begin to decrease over time. The uncontrollable muscle movements may disappear entirely, but the episodes of hemiplegia occur throughout life.

Alternating hemiplegia of childhood also causes mild to severe cognitive problems. Almost all affected individuals have some level of developmental delay and intellectual disability. Their cognitive functioning typically declines over time.

### Frequency

Alternating hemiplegia of childhood is a rare condition that affects approximately 1 in 1 million people.

### Causes

Alternating hemiplegia of childhood is primarily caused by mutations in the *ATP1A3* gene. Very rarely, a mutation in the *ATP1A2* gene is involved in the condition. These genes provide instructions for making very similar proteins. They function as different forms of one piece, the alpha subunit, of a larger protein complex called Na<sup>+</sup>/K<sup>+</sup> ATPase; the two versions of the complex are found in different parts of the brain. Both versions play a critical role in the normal function of nerve cells (neurons). Na<sup>+</sup>/K<sup>+</sup> ATPase transports charged atoms (ions) into and out of neurons, which is an essential part of the signaling process that controls muscle movement.

Mutations in the *ATP1A3* or *ATP1A2* gene reduce the activity of the Na<sup>+</sup>/K<sup>+</sup> ATPase, impairing its ability to transport ions normally. It is unclear how a malfunctioning Na<sup>+</sup>/K<sup>+</sup> ATPase causes the episodes of paralysis or uncontrollable movements characteristic of alternating hemiplegia of childhood.

## **Inheritance Pattern**

Alternating hemiplegia of childhood is considered an autosomal dominant condition, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Most cases of alternating hemiplegia of childhood result from new mutations in the gene and occur in people with no history of the disorder in their family. However, the condition can also run in families. For unknown reasons, the signs and symptoms are typically milder when the condition is found in multiple family members than when a single individual is affected.

## **Other Names for This Condition**

- alternating hemiplegia syndrome

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/genetictesting](#)
- Genetic Testing Registry: Alternating hemiplegia of childhood 1  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3549447/>
- Genetic Testing Registry: Alternating hemiplegia of childhood 2  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3553788/>

### Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22alternating+hemiplegia+of+childhood%22>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Encyclopedia: Movement - Uncontrollable  
<https://medlineplus.gov/ency/article/003201.htm>
- Encyclopedia: Muscle Function Loss  
<https://medlineplus.gov/ency/article/003190.htm>

- Health Topic: Neurologic Diseases  
<https://medlineplus.gov/neurologicdiseases.html>
- Health Topic: Paralysis  
<https://medlineplus.gov/paralysis.html>

#### Genetic and Rare Diseases Information Center

- Alternating hemiplegia of childhood  
<https://rarediseases.info.nih.gov/diseases/11/alternating-hemiplegia-of-childhood>

#### Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Alternating Hemiplegia Information Page  
<https://www.ninds.nih.gov/Disorders/All-Disorders/Alternating-Hemiplegia-Information-Page>

#### Educational Resources

- MalaCards: alternating hemiplegia of childhood  
[https://www.malacards.org/card/alternating\\_hemiplegia\\_of\\_childhood](https://www.malacards.org/card/alternating_hemiplegia_of_childhood)
- Orphanet: Alternating hemiplegia of childhood  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=2131](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2131)

#### Patient Support and Advocacy Resources

- Alternating Hemiplegia of Childhood Foundation  
<http://ahckids.org/>
- Cure AHC  
<http://cureahc.org/>
- National Organization for Rare Disorders  
<https://rarediseases.org/rare-diseases/alternating-hemiplegia-of-childhood/>
- Rare Connect  
<https://www.rareconnect.org/en/community/alternating-hemiplegia>

#### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Hemiplegia%5BMAJR%5D%29+AND+%28alternating+hemiplegia+of+childhood%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

## Catalog of Genes and Diseases from OMIM

- ALTERNATING HEMIPLEGIA OF CHILDHOOD 1  
<http://omim.org/entry/104290>
- ALTERNATING HEMIPLEGIA OF CHILDHOOD 2  
<http://omim.org/entry/614820>

## Sources for This Summary

- Bassi MT, Bresolin N, Tonelli A, Nazos K, Crippa F, Baschiroto C, Zucca C, Bersano A, Dolcetta D, Boneschi FM, Barone V, Casari G. A novel mutation in the ATP1A2 gene causes alternating hemiplegia of childhood. *J Med Genet.* 2004 Aug;41(8):621-8.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/15286158>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735877/>
- Heinzen EL, Swoboda KJ, Hitomi Y, Gurrieri F, Nicole S, de Vries B, Tiziano FD, Fontaine B, Walley NM, Heavin S, Panagiotakaki E; European Alternating Hemiplegia of Childhood (AHC) Genetics Consortium; Biobanca e Registro Clinico per l'Emiplegia Alternante (I.B.AHC) Consortium; European Network for Research on Alternating Hemiplegia (ENRAH) for Small and Medium-sized Enterprise (SMEs) Consortium, Fiori S, Abiusi E, Di Pietro L, Sweney MT, Newcomb TM, Viollet L, Huff C, Jorde LB, Reyna SP, Murphy KJ, Shianna KV, Gumbs CE, Little L, Silver K, Ptáček LJ, Haan J, Ferrari MD, Bye AM, Herkes GK, Whitelaw CM, Webb D, Lynch BJ, Uldall P, King MD, Scheffer IE, Neri G, Arzimanoglou A, van den Maagdenberg AM, Sisodiya SM, Mikati MA, Goldstein DB. De novo mutations in ATP1A3 cause alternating hemiplegia of childhood. *Nat Genet.* 2012 Sep; 44(9):1030-4. doi: 10.1038/ng.2358. Epub 2012 Jul 29.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/22842232>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3442240/>
- Panagiotakaki E, De Grandis E, Stagnaro M, Heinzen EL, Fons C, Sisodiya S, de Vries B, Goubau C, Weckhuysen S, Kemlink D, Scheffer I, Lesca G, Rabilloud M, Klich A, Ramirez-Camacho A, Ulate-Campos A, Campistol J, Giannotta M, Moutard ML, Doummar D, Hubsch-Bonneaud C, Jaffer F, Cross H, Gurrieri F, Tiziano D, Nevsimalova S, Nicole S, Neville B, van den Maagdenberg AM, Mikati M, Goldstein DB, Vavassori R, Arzimanoglou A; Italian IBAHC Consortium; French AHC Consortium; International AHC Consortium. Clinical profile of patients with ATP1A3 mutations in Alternating Hemiplegia of Childhood—a study of 155 patients. *Orphanet J Rare Dis.* 2015 Sep 26;10: 123. doi: 10.1186/s13023-015-0335-5.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/26410222>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4583741/>
- Rosewich H, Thiele H, Ohlenbusch A, Maschke U, Altmüller J, Frommolt P, Zirn B, Ebinger F, Siemes H, Nürnberg P, Brockmann K, Gärtner J. Heterozygous de-novo mutations in ATP1A3 in patients with alternating hemiplegia of childhood: a whole-exome sequencing gene-identification study. *Lancet Neurol.* 2012 Sep;11(9):764-73. doi: 10.1016/S1474-4422(12)70182-5. Epub 2012 Jul 30.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/22850527>
- Sweney MT, Silver K, Gerard-Blanluet M, Pedespan JM, Renault F, Arzimanoglou A, Schlesinger-Massart M, Lewelt AJ, Reyna SP, Swoboda KJ. Alternating hemiplegia of childhood: early characteristics and evolution of a neurodevelopmental syndrome. *Pediatrics.* 2009 Mar;123(3): e534-41. doi: 10.1542/peds.2008-2027.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/19254988>

---

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/alternating-hemiplegia-of-childhood>

Reviewed: September 2016  
Published: August 17, 2020

Lister Hill National Center for Biomedical Communications  
U.S. National Library of Medicine  
National Institutes of Health  
Department of Health & Human Services