

Anophthalmia/microphthalmia-esophageal atresia syndrome

Description

Anophthalmia/microphthalmia-esophageal atresia (AEG) syndrome is a rare disorder that is characterized by the abnormal development of the eyes and other parts of the body, including the tube that carries food from the mouth to the stomach (esophagus).

People who have AEG syndrome are usually born without one or both eyes (anophthalmia), although some individuals have underdeveloped and abnormally small eyes (microphthalmia). People who have anophthalmia have no vision in the affected eye, but people who have microphthalmia may or may not have significant vision loss.

Affected individuals who have some remaining eye tissue can have additional eye abnormalities. Some people may be missing pieces of tissue in the structures that form the eye (coloboma), or the nerves that carry signals between the eyes and the brain may be underdeveloped (optic nerve hypoplasia). The presence of other eye problems can worsen an affected person's vision.

Some people with AEG syndrome are born with a blocked esophagus (esophageal atresia), which is often accompanied by an abnormal connection between the windpipe (trachea) and the esophagus (tracheoesophageal fistula). Additional features of AEG syndrome can include brain abnormalities, slow growth, delayed development of motor skills (such as walking), and intellectual disabilities. Affected individuals may also have genital abnormalities, which can include undescended testes (cryptorchidism) and an unusually small penis.

Frequency

AEG syndrome is estimated to affect 1 in 250,000 individuals.

Causes

Variants (also called mutations) in the *SOX2* gene cause AEG syndrome. This gene provides instructions for making a protein that regulates the activity of other genes, including those that are important for the normal development of the eyes.

The *SOX2* protein plays a critical role in the formation of many different tissues and organs during embryonic development. Variants in the *SOX2* gene can cause cells to produce a version of the *SOX2* protein that does not function properly. As a result, the

protein cannot regulate the activity of genes that are essential for the development of the eyes and other parts of the body. Abnormal development of these structures causes the signs and symptoms of AEG syndrome.

[Learn more about the gene associated with Anophthalmia/microphthalmia-esophageal atresia syndrome](#)

- SOX2

Inheritance

AEG syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Most cases of this condition result from new (*de novo*) variants in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or during early embryonic development. These affected individuals typically have no history of the disorder in their family.

In a small number of cases, people with AEG syndrome have inherited the altered gene from an unaffected parent who has a SOX2 variant only in their sperm or egg cells. This phenomenon is called germline mosaicism.

Other Names for This Condition

- AEG syndrome
- Anophthalmia-esophageal-genital syndrome
- MCOPS3
- SOX2 anophthalmia syndrome
- SOX2 disorder
- SOX2 syndrome
- SOX2-related eye disorders
- Syndromic microphthalmia type 3

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Anophthalmia/microphthalmia-esophageal atresia syndrome (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1859773/>)

Genetic and Rare Diseases Information Center

- Anophthalmia/microphthalmia-esophageal atresia syndrome (<https://rarediseases.in>)

fo.nih.gov/diseases/1443/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- MICROPHTHALMIA, SYNDROMIC 3; MCOPS3 (<https://omim.org/entry/206900>)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=Anophthalmia-esophageal+atresia+syndrome+OR+SOX2+anophthalmia+syndrome+OR+MCOPS3&filter=date+arch.y_10)

References

- Bakrania P, Robinson DO, Bunyan DJ, Salt A, Martin A, Crolla JA, Wyatt A, Fielder A, Ainsworth J, Moore A, Read S, Uddin J, Laws D, Pascuel-Salcedo D, Ayuso C, Allen L, Collin JR, Ragge NK. SOX2 anophthalmia syndrome: 12 new cases demonstrating broader phenotype and high frequency of large gene deletions. *Br J Ophthalmol*. 2007 Nov;91(11):1471-6. doi: 10.1136/bjo.2007.117929. Epub 2007 May 23. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17522144>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2095460/>)
- Kelberman D, de Castro SC, Huang S, Crolla JA, Palmer R, Gregory JW, Taylor D, Cavallo L, Faienza MF, Fischetto R, Achermann JC, Martinez-Barbera JP, Rizzoti K, Lovell-Badge R, Robinson IC, Gerrelli D, Dattani MT. SOX2 plays a critical role in the pituitary, forebrain, and eye during human embryonic development. *J Clin Endocrinol Metab*. 2008 May;93(5):1865-73. doi: 10.1210/jc.2007-2337. Epub 2008 Feb 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18285410>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3479085/>)
- Schneider A, Bardakjian TM, Zhou J, Hughes N, Keep R, Dorsainville D, Kherani F, Katowitz J, Schimmenti LA, Hummel M, Fitzpatrick DR, Young TL. Familial recurrence of SOX2 anophthalmia syndrome: phenotypically normal mother with two affected daughters. *Am J Med Genet A*. 2008 Nov 1;146A(21):2794-8. doi: 10.1002/ajmg.a.32384. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18831064>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3693575/>)
- Tziaferi V, Kelberman D, Dattani MT. The role of SOX2 in hypogonadotropic hypogonadism. *Sex Dev*. 2008;2(4-5):194-9. doi: 10.1159/000152035. Epub 2008 Nov 5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18987493>)

- Verma AS, Fitzpatrick DR. Anophthalmia and microphthalmia. *Orphanet J RareDis*. 2007 Nov 26;2:47. doi: 10.1186/1750-1172-2-47. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18039390>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2246098/>)
- Williamson KA, FitzPatrick DR. The genetic architecture of microphthalmia, anophthalmia and coloboma. *Eur J Med Genet*. 2014 Aug;57(8):369-80. doi:10.1016/j.ejmg.2014.05.002. Epub 2014 May 22. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24859618>)
- Williamson KA, Hever AM, Rainger J, Rogers RC, Magee A, Fiedler Z, Keng WT, Sharkey FH, McGill N, Hill CJ, Schneider A, Messina M, Turnpenny PD, Fantes JA, van Heyningen V, FitzPatrick DR. Mutations in SOX2 cause anophthalmia-esophageal-genital (AEG) syndrome. *Hum Mol Genet*. 2006 May1;15(9):1413-22. doi: 10.1093/hmg/ddl064. Epub 2006 Mar 16. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16543359>)
- Williamson KA, Yates TM, FitzPatrick DR. SOX2 Disorder. 2006 Feb 23[updated 2020 Jul 30]. In: Adam MP, Bick S, Mirzaa GM, Wallace SE, Amemiya A, editors. *GeneReviews(R)* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1300/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301477>)
- Zhou J, Kherani F, Bardakjian TM, Katowitz J, Hughes N, Schimmenti LA, Schneider A, Young TL. Identification of novel mutations and sequence variants in the SOX2 and CHX10 genes in patients with anophthalmia/microphthalmia. *Mol Vis*. 2008 Mar 24;14:583-92. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18385794>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2275209/>)

Last updated July 2, 2025