Anophthalmia/Microphthalmia

Description

Anophthalmia and microphthalmia are disorders that affect eye development before birth. Microphthalmia is a birth defect in which one or both eyes do not develop fully and are abnormally small. Anophthalmia is a more severe birth defect in which one or both eyes do not form at all. While people who have anophthalmia have no vision in the affected eye, people who have microphthalmia may or may not have significant vision loss. Because both conditions are characterized by impaired eye development, anophthalmia and microphthalmia are often considered to be related disorders (anophthalmia/microphthalmia).

Anophthalmia and microphthalmia can occur along with other eye abnormalities. People who have one missing eye (unilateral anophthalmia) can have additional eye abnormalities in the unaffected eye, while people who have microphthalmia can have additional eye abnormalities in one or both eyes (complex microphthalmia). The presence of other eye problems can worsen vision. Additional eye abnormalities can include a missing piece of tissue that may appear as a notch or gap in one of several parts of the eye (coloboma); a clouding of the lens of the eye (cataract); abnormal development of the cells in the retina (retinal dysplasia); or microcornea, in which the clear front covering of the eye (cornea) is small and abnormally curved.

Some individuals have anophthalmia or microphthalmia as part of a syndrome that affects multiple parts of the body (syndromic anophthalmia or microphthalmia). As many as 45 percent of people with anophthalmia or microphthalmia have the condition as part of a recognized syndrome, such as CHARGE syndrome, Fraser syndrome type 1 or 2, and oculofaciocardiodental syndrome. When people have anophthalmia or microphthalmia but do not have additional abnormalities of the eye or other body systems, this is known as isolated anophthalmia or microphthalmia.

Frequency

Microphthalmia occurs in approximately 1 in 7,000 people, while anophthalmia occurs in approximately 1 in 30,000 people.

Causes

Variants (also called mutations) in one of the many genes that are involved in the early

development of the eye can cause anophthalmia or microphthalmia. Researchers believe that variants in as many as 90 different genes may cause these conditions. Many of the genes that are associated with anophthalmia and microphthalmia have been identified in only a very small number of affected individuals.

A genetic variant is more likely to be found in individuals who have anophthalmia or severe microphthalmia that affects both eyes (bilateral). Variants in the *SOX2* gene are found in approximately 10 to 15 percent of these cases. Variants in many other genes account for a small percentage of cases. Together, variants in the *SOX2* and *OTX2* genes are believed to cause more than half of all cases of bilateral anophthalmia or bilateral and severe microphthalmia.

Some people who have anophthalmia or microphthalmia have a change in the number or structure of chromosomes. Occasionally, environmental factors that affect the development of the eyes before birth, such as a shortage of certain vitamins, infections such as rubella, or exposure to substances that cause birth defects (teratogens), can cause anophthalmia or microphthalmia

Learn more about the genes associated with Anophthalmia/Microphthalmia

- ALX1
- BCOR
- CHD7
- COL4A1
- FRAS1
- GDF3
- GDF6
- GJA1
- HCCS
- KMT2D
- LRP5
- MITF
- NDP
- OTX2
- PAX6
- PORCN
- PQBP1
- RERE
- SALL1
- SALL4
- SHH
- SMCHD1

- SMOC1
- SOX2
- TFAP2A

Additional Information from NCBI Gene:

- ABCB6
- ALDH1A3
- ATOH7
- BMP4
- BMP7
- C12orf57
- COX7B
- CRYAA
- CRYBA4
- FNBP4
- FOXE3
- GJA8
- GLI2
- HMGB3
- HMX1
- MAB21L2
- MAF
- MFRP
- NAA10
- NDUFB11
- NHS
- PITX3
- PRSS56
- PXDN
- RAB3GAP1
- RARB
- RAX
- RBP4
- RPGRIP1L
- SIX6
- STRA6

- TBC1D32
- TENM3
- TMX3
- VAX1
- VSX2
- YAP1

Inheritance

Anophthalmia and microphthalmia can be inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Many cases 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, an unaffected parent has the variant only in their sperm or egg cells. This phenomenon is called germline mosaicism. Cases of anophthalmia or microphthalmia that are caused by variants in the *SOX2* and *OTX2* genes are typically inherited in an autosomal dominant pattern.

Anophthalmia and microphthalmia can also be 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, but they typically do not show signs and symptoms of the condition.

In some families, the conditions are inherited in an X-linked pattern. A condition is considered X-linked if the altered gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. In males (who have only one X chromosome) a variant in the only copy of the gene in each cell is typically sufficient to cause the condition. In females (who have two copies of the X chromosome) one altered copy of the gene may or may not cause features of the condition. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

When the conditions occur as part of another syndrome, they follow the inheritance pattern of that syndrome.

Cases of anophthalmia or microphthalmia that are caused by environmental factors are not inherited.

Other Names for This Condition

- A/M
- Anophthalmia
- Anophthalmos

- Microphthalmia
- Microphthalmos

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Anophthalmia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0003119/)
- Genetic Testing Registry: Microphthalmia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0026010/)

Genetic and Rare Diseases Information Center

- Isolated microphthalmia-anophthalmia-coloboma (https://rarediseases.info.nih.gov/diseases/12085/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Anophthalmia/Microphthalmia%22)

Catalog of Genes and Diseases from OMIM

- MICROPHTHALMIA, SYNDROMIC 2; MCOPS2 (https://omim.org/entry/300166)
- MICROPHTHALMIA, SYNDROMIC 9; MCOPS9 (https://omim.org/entry/601186)
- MICROPHTHALMIA, SYNDROMIC 8; MCOPS8 (https://omim.org/entry/601349)
- MICROPHTHALMIA, SYNDROMIC 3; MCOPS3 (https://omim.org/entry/206900)
- MICROPHTHALMIA, ISOLATED 1; MCOP1 (https://omim.org/entry/251600)
- MICROPHTHALMIA, SYNDROMIC 1; MCOPS1 (https://omim.org/entry/309800)
- MICROPHTHALMIA, SYNDROMIC 13; MCOPS13 (https://omim.org/entry/300915)
- MICROPHTHALMIA, SYNDROMIC 6; MCOPS6 (https://omim.org/entry/607932)
- MICROPHTHALMIA, ISOLATED 2; MCOP2 (https://omim.org/entry/610093)
- MICROPHTHALMIA, SYNDROMIC 5; MCOPS5 (https://omim.org/entry/610125)
- MICROPHTHALMIA, SYNDROMIC 10; MCOPS10 (https://omim.org/entry/611222)
- MICROPHTHALMIA, SYNDROMIC 16; MCOPS16 (https://omim.org/entry/611038)

- MICROPHTHALMIA, ISOLATED 5; MCOP5 (https://omim.org/entry/611040)
- MICROPHTHALMIA, ISOLATED 6; MCOP6 (https://omim.org/entry/613517)
- MICROPHTHALMIA, ISOLATED 8; MCOP8 (https://omim.org/entry/615113)
- MICROPHTHALMIA, ISOLATED 7; MCOP7 (https://omim.org/entry/613704)
- MICROPHTHALMIA, SYNDROMIC 12; MCOPS12 (https://omim.org/entry/615524)
- MICROPHTHALMIA, ISOLATED 4; MCOP4 (https://omim.org/entry/613094)
- MICROPHTHALMIA, SYNDROMIC 11; MCOPS11 (https://omim.org/entry/614402)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28microphthalmia%5BTI%5D%29+OR+%28anophthalmia%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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