Stickler syndrome

Description

Stickler syndrome is a group of hereditary conditions that are characterized by a distinctive facial appearance, eye abnormalities, hearing loss, and joint problems. These signs and symptoms vary widely among affected individuals, even among members of the same family.

A characteristic feature of Stickler syndrome is a flattened facial appearance that results from underdeveloped bones in the middle of the face. A particular group of physical features called Pierre Robin sequence is also common in people with Stickler syndrome. Pierre Robin sequence includes an opening in the roof of the mouth (a cleft palate), a tongue that is placed further back than normal (glossoptosis), and a small lower jaw (micrognathia). This combination of features can lead to feeding problems and difficulty breathing after birth.

Many individuals with Stickler syndrome have severe nearsightedness (high myopia), which means they have trouble seeing things that are far away. In some cases, the clear gel that fills the eyeball (the vitreous) has an abnormal appearance, which is noticeable during an eye examination. Other eye problems are also common in people with Stickler syndrome, including increased pressure within the eye (glaucoma), clouding of the lens of the eyes (cataracts), and tearing of the light-sensitive tissue at the back of the eye (retinal detachment). These eye abnormalities can impair vision and may lead to blindness.

Hearing loss is also common in people with Stickler syndrome. In affected individuals, the degree of hearing loss can vary and may worsen over time. People with Stickler syndrome typically have sensorineural hearing loss (caused by changes in the inner ear) with or without conductive hearing loss (caused by changes in the middle ear).

Most people with Stickler syndrome have joint abnormalities. Arthritis often develops early in life and may cause joint pain or stiffness. People with severe joint disease may need surgery to replace damaged joints in their 20s or 30s. Affected individuals may also have abnormal curvature of the spine (scoliosis or kyphosis) that causes back pain.

Researchers have described several types of Stickler syndrome, which are distinguished by their genetic causes, features, and patterns of inheritance. In particular, the eye abnormalities and severity of hearing loss vary among the different types. Some types of Stickler syndrome are very rare and have been diagnosed in only a few

individuals.

Frequency

Stickler syndrome affects an estimated 1 in 7,500 to 9,000 newborns.

Causes

Variants (also called mutations) in several genes cause the different types of Stickler syndrome. Approximately 80 percent of people with Stickler syndrome have a variant in the *COL2A1* gene. Variants in the *COL11A1* gene are the next most common cause of Stickler syndrome.

The most common genes associated with Stickler syndrome are called collagen genes because they provide instructions for making components of collagens. Collagens are complex molecules that give structure and strength to the connective tissues that support the body's joints and organs. Variants in the collagen genes impair the production, processing, or assembly of collagen molecules. Altered collagen molecules or reduced amounts of collagen impair the development of connective tissues in many different parts of the body, leading to the varied features of Stickler syndrome.

In rare cases, individuals with signs and symptoms similar to those seen in people with Stickler syndrome have been found to have variants in genes that are not involved in collagen production. Researchers are working to learn more about these genes and their possible association with Stickler syndrome.

Learn more about the genes associated with Stickler syndrome

- COL11A1
- COL11A2
- COL2A1
- COL9A1
- COL9A2
- COL9A3

Inheritance

Most often, Stickler syndrome is inherited inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. This includes cases of Stickler syndrome that are caused by variants in the *COL2A1*, *COL11A1*, and *COL11A2* genes. Sometimes, Stickler syndrome is the result of a new (de novo) variant in the gene that occurs during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or during early embryonic development. These affected individuals have no history of the disorder in their family.

When Stickler syndrome is caused by variants in other genes, it can 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.

Other Names for This Condition

- Arthroophthalmopathy
- Hereditary arthro-ophthalmo-dystrophy
- Hereditary arthro-ophthalmopathy
- Stickler dysplasia

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Otospondylomegaepiphyseal dysplasia, autosomal dominant (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848488/)
- Genetic Testing Registry: Marshall syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265235/)
- Genetic Testing Registry: Stickler syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265253/)
- Genetic Testing Registry: Stickler syndrome type 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2020284/)
- Genetic Testing Registry: Stickler syndrome type 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1858084/)
- Genetic Testing Registry: Stickler syndrome, type 4 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3279941/)
- Genetic Testing Registry: Stickler syndrome, type 5 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3280342/)

Genetic and Rare Diseases Information Center

- Stickler syndrome (https://rarediseases.info.nih.gov/diseases/10782/index)

Patient Support and Advocacy Resources

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

Clinical Trials

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

Catalog of Genes and Diseases from OMIM

- STICKLER SYNDROME, TYPE I; STL1 (https://omim.org/entry/108300)
- OTOSPONDYLOMEGAEPIPHYSEAL DYSPLASIA, AUTOSOMAL DOMINANT; OSMEDA (https://omim.org/entry/184840)
- STICKLER SYNDROME, TYPE II; STL2 (https://omim.org/entry/604841)
- STICKLER SYNDROME, TYPE I, NONSYNDROMIC OCULAR (https://omim.org/entry/609508)
- STICKLER SYNDROME, TYPE V; STL5 (https://omim.org/entry/614284)
- STICKLER SYNDROME, TYPE IV; STL4 (https://omim.org/entry/614134)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28Stickler+syndrome%5BTIAB%5D%29+OR+%28arthro-ophthalmopathy%5BTIAB%5D%29+OR+%28Marshall+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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