STICKLER SYNDROME

Otherwise known as?

Stickler syndrome is also known by the following names:

1. Hereditary Progressive Arthro-ophthalmopathy – This name highlights the condition's primary features, including arthropathy (joint problems) and ophthalmopathy (eye issues).

2. Stickler Collagenopathy – This name emphasizes the condition's genetic cause, as it is linked to reduced collagen production.

3. Stickler Syndrome Type I, Type II, Type III – Referring to the different subtypes of the syndrome, based on the specific genetic mutations involved (e.g., mutations in COL2A1, COL11A1, and COL11A2 genes).

Signs & Symptoms

Stickler syndrome is a genetic condition that primarily affects the connective tissues in the body, leading to a variety of issues with the joints, eyes, hearing, and sometimes the facial structure. The severity of symptoms can vary widely among individuals, but common signs and symptoms include:

1. Ocular (Eye) Problems

Stickler syndrome often causes a range of eye issues due to differences in the connective tissue in the eyes:

- Myopia (near sightedness): One of the most common symptoms, leading to difficulty seeing objects at a distance.
- Retinal Problems: Individuals with Stickler syndrome are at increased risk for retinal detachment and retinal holes, which can lead to vision loss if not treated.
- Cataracts: Early development of cataracts, which causes clouding of the lens in the eye and can lead to blurry vision.
- Glaucoma: Increased pressure in the eye that can damage the optic nerve, potentially leading to vision loss.

2. Joint and Skeletal Problems

The syndrome can cause joint problems and skeletal anomalies, leading to:

- Arthritis: Many individuals with Stickler syndrome experience early-onset arthritis due to differences in cartilage and bone development. This can lead to joint pain, stiffness, and decreased mobility.

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- Hypermobile Joints: The connective tissue can cause joint hypermobility, where joints are more flexible than normal, leading to an increased risk of dislocations and joint pain.
- Cleft Palate or Cleft Lip: A significant number of individuals with Stickler syndrome may have a cleft palate, which affects the roof of the mouth and can lead to feeding, speech, and hearing difficulties.
- Scoliosis: Some people may develop curvature of the spine (scoliosis) as they grow older.

3. Hearing Problems

Stickler syndrome can also affect the ears, leading to hearing difficulties:

- Sensorineural Hearing Loss: This is a common feature, where there is damage to the inner ear or the nerve pathways involved in hearing. The severity of hearing loss can vary, and some individuals may require hearing aids.
- Conductive Hearing Loss: Due to differences in the ear structures, conductive hearing loss can also occur, where sound is not conducted properly through the ear canal.

4. Facial Features

People with Stickler syndrome may exhibit distinctive facial features due to the connective tissue differences:

- Flattened Face: A somewhat flat or underdeveloped midface with a relatively flat nose.
- Small Chin (Micrognathia): A smaller-than-normal lower jaw, leading to a receded chin appearance.
- Prominent Eyes: The eyes may appear more prominent due to facial bones developing differently.
- Broad, Flattened Nose Bridge: Some people may have a broader and flattened nose bridge.

5. Other Possible Symptoms

- Short Stature: Some individuals may experience short stature or delayed growth due to issues with bone development and cartilage.
- Heart Problems: In rare cases, individuals with Stickler syndrome may have heart problems, including valvular irregularities or aortic dilation.
- Difficulty with Feeding or Swallowing: Due to the cleft palate, infants with Stickler syndrome may have trouble feeding properly.

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6. Other Complications

- Sleep Apnoea: The differences in the upper airway, including the cleft palate, can cause sleep apnoea, which is a condition where breathing is repeatedly interrupted during sleep.
- Breathing Issues: In some cases, particularly when a cleft palate is present, individuals may experience difficulty breathing, especially during infancy.

Causes

Stickler syndrome is a genetic condition caused by mutations in certain genes that affect the production and function of collagen, a key protein in the connective tissues of the body. These genetic mutations interfere with the normal development of connective tissues in the eyes, joints, bones, and other parts of the body. The condition is typically inherited in an autosomal dominant pattern, meaning only one copy of the mutated gene is required.

1. Genetic Mutations in Collagen Genes

Stickler syndrome is caused by mutations in the genes that code for collagen, a major protein in connective tissues. There are several different genetic mutations that can lead to Stickler syndrome, affecting different types of collagen:

- COL2A1 Gene Mutation: The majority of individuals with Stickler syndrome have mutations in the COL2A1 gene, which codes for type II collagen. Type II collagen is primarily found in the cartilage, eye, and inner ear, so mutations in this gene lead to the typical features of ocular problems (such as retinal detachment), joint problems, and hearing loss.
- COL11A1 Gene Mutation: Some cases of Stickler syndrome are due to mutations in the COL11A1 gene, which produces type XI collagen. This type of collagen is found in tissues such as cartilage, bone, and the eye. Mutations in COL11A1 may lead to similar features but can also cause hearing loss and other craniofacial differences.
- COL11A2 Gene Mutation: A smaller subset of Stickler syndrome cases is caused by mutations in the COL11A2 gene, which also codes for type XI collagen. Mutations in this gene typically affect the inner ear, cartilage, and eye.

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2. Inheritance Pattern

Stickler syndrome is inherited in an autosomal dominant manner, which means that a person only needs one copy of the mutated gene to develop the condition. An affected individual has a 50% chance of passing the mutated gene to their child.

- Inherited from an affected parent: If one parent has Stickler syndrome, there is a 50% chance that the child will inherit the mutated gene and develop the syndrome.
- De novo mutations: In some cases, Stickler syndrome may occur due to a new (de novo) mutation in the gene, meaning it is not inherited from either parent but arises spontaneously in the individual.

3. Other Genetic Factors

While the primary cause of Stickler syndrome is mutations in the COL2A1, COL11A1, or COL11A2 genes, other genetic changes or modifiers may influence the severity and presentation of the condition. In rare instances, additional genetic or environmental factors may contribute to the phenotype.

Testing & Diagnosis

Diagnosing Stickler syndrome involves a combination of clinical evaluation, genetic testing, and sometimes imaging studies to confirm the presence of characteristic features and mutations.

1. Clinical Evaluation

The diagnosis often starts with a thorough clinical assessment to look for the characteristic features of Stickler syndrome, which can vary widely in severity from person to person. The doctor will review the individual's medical history, family history, and physical features.

Clinical features to look for:

- Ocular Symptoms: Common issues include myopia (near sightedness), retinal problems (such as retinal detachment, retinal holes, or retinal degeneration), cataracts, and glaucoma.
- Skeletal Anomalies: These may include joint hypermobility, early-onset arthritis, scoliosis, and flattened facial features (such as a small jaw or flat nose).

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- Hearing Loss: Sensorineural or conductive hearing loss can occur, often due to differences in the inner ear or middle ear structures.
- Cleft Palate: A cleft palate is present in a significant proportion of individuals with Stickler syndrome.

2. Genetic Testing

Genetic testing is crucial for confirming the diagnosis of Stickler syndrome, especially to identify mutations in the collagen genes (which are responsible for the condition).

Types of Genetic Tests:

- DNA Sequencing: This is the most definitive test. It looks for mutations in the COL2A1, COL11A1, and COL11A2 genes, which are associated with Stickler syndrome.
  - COL2A1 mutations are the most common cause and are typically associated with more severe eye and joint problems.
  - COL11A1 and COL11A2 mutations can also cause the syndrome, but they may result in slightly different clinical features, including specific eye and ear problems.
- Chromosomal Microarray: This test may be used to detect larger deletions or duplications in the collagen genes or other associated regions of the genome.
- Familial Testing: If a family member has been diagnosed with Stickler syndrome, genetic testing can confirm whether the same mutation is present in other family members, which can help in predicting inheritance patterns and determining the risk for future generations.

3. Imaging Studies

Imaging tests may be used to examine the skeletal, ocular, and ear features of the syndrome:

- Ophthalmological Exam: An ophthalmologist will typically conduct a comprehensive eye exam to look for signs of myopia, retinal detachment, cataracts, and glaucoma. Special tests, such as retinal imaging, may be done to assess the condition of the retina.
- Skeletal Imaging: X-rays, MRI, or CT scans may be used to assess joint differences, scoliosis, cleft palate, or other bone anomalies associated with Stickler syndrome.
  - X-rays may be used to look for joint problems (like arthritis or joint hypermobility), skeletal dysplasia, or spinal differences.
  - MRI or CT scans may provide a more detailed look at craniofacial structures and joint differences.

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4. Audiological Testing

Since hearing loss is a common feature of Stickler syndrome, hearing tests are an important part of the diagnostic process. Tests may include:

- Audiometry: This measures the ability to hear different sounds and tones. It helps assess the type and degree of hearing loss (sensorineural or conductive).
- Otoacoustic Emissions (OAE): This test assesses the function of the inner ear, specifically the cochlea.
- Auditory Brainstem Response (ABR): This test measures how the ear and brain respond to sounds and can help assess nerve-related hearing loss.

5. Family History and Genetic Counselling

Since Stickler syndrome is inherited in an autosomal dominant pattern, genetic counselling plays an important role in helping affected families understand the inheritance patterns. Family members may undergo genetic testing to see if they carry the mutation, especially if a close relative is diagnosed with the condition.

- Genetic Counselling: A counsellor can explain the chances of passing on the condition to future children, guide families on potential reproductive options, and help interpret genetic test results.

Treatment

There is no cure for Stickler syndrome, as it is a genetic condition. However, treatment focuses on managing symptoms and preventing complications. A multidisciplinary approach involving specialists in ophthalmology, orthopaedics, audiology, and genetics is essential for managing the condition. Treatment plans vary depending on the severity of symptoms and the individual's specific needs.

1. Ocular (Eye) Treatment

Stickler syndrome often causes eye problems, such as retinal detachment, myopia (near sightedness), cataracts, and glaucoma. Regular eye examinations by an ophthalmologist are essential to monitor and treat these issues.

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- Retinal Detachment: Individuals with Stickler syndrome are at increased risk for retinal detachment, which can cause vision loss. Regular eye exams can help detect retinal changes early. If retinal detachment occurs, it may require surgical intervention (e.g., laser therapy or cryotherapy).
- Cataracts: Early cataracts may be treated with surgical removal of the cloudy lens, followed by intraocular lens implantation to restore vision.
- Glaucoma: If glaucoma develops, it may be treated with medications to lower eye pressure, or surgical procedures in more severe cases.
- Myopia: Corrective measures like glasses or contact lenses can help manage near sightedness.
- Regular Monitoring: Individuals should have regular eye exams to check for new or worsening eye problems.

2. Joint and Skeletal Management

Joint problems, such as arthritis and hypermobile joints, are common in Stickler syndrome. Treatment focuses on relieving pain and improving mobility:

- Pain Management: Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen can help reduce inflammation and relieve joint pain.
- Physiotherapy: A physical therapist can design exercises to improve joint flexibility and strength, reduce pain, and prevent further joint damage.
- Orthopaedic Interventions: In cases of severe joint problems, surgery may be needed to address hip dysplasia, scoliosis, or other skeletal differences.
- Supportive Devices: Braces or splints may be used to support hypermobile joints or prevent injury.
- Management of Scoliosis: In some cases, individuals with scoliosis may need a back brace or, in severe cases, spinal surgery to address the curvature.

3. Hearing Loss Management

Since hearing loss is common in Stickler syndrome, hearing tests should be performed regularly to assess the degree and type of hearing impairment. Treatment options include:

- Hearing Aids: Hearing aids can help amplify sounds for individuals with sensorineural hearing loss or conductive hearing loss.
- Cochlear Implants: In cases of severe hearing loss that cannot be improved with hearing aids, cochlear implants may be considered. These devices bypass damaged parts of the ear and directly stimulate the auditory nerve.
- Regular Hearing Tests: Frequent hearing assessments by an audiologist are essential to monitor the progression of hearing loss.

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4. Cleft Palate Treatment

Many individuals with Stickler syndrome have a cleft palate or cleft lip, which may affect speech and feeding, especially in infants.

- Surgical Repair: Cleft palate repair surgery is usually performed in infancy to close the gap in the roof of the mouth. This surgery improves feeding, speech, and reduces the risk of ear infections.
- Speech Therapy: After the repair, speech therapy may be necessary to help the child learn speech and language skills, especially if the palate repair is delayed.
- Dental Care: Children with a cleft palate often need specialized dental care to manage the development of teeth and oral structures.

5. Genetic Counselling

Genetic counselling is an important part of the treatment process, especially for families who have a history of Stickler syndrome.

- Understanding Inheritance: Genetic counselling helps families understand the autosomal dominant inheritance pattern of Stickler syndrome and the risk of passing the condition to future children.
- Family Testing: Family members of an affected individual may be tested to identify whether they carry the same genetic mutation, allowing for early intervention and monitoring.

6. Multidisciplinary Care

Given the variety of symptoms involved in Stickler syndrome, it is crucial to involve multiple specialists in the treatment plan:

- Ophthalmologist: For ongoing eye care, including monitoring for retinal detachment, cataracts, and other vision-related issues.
- Orthopaedic Specialist: To manage joint issues, arthritis, and skeletal differences.
- Audiologist: For hearing assessments and management, including hearing aids or cochlear implants.
- Geneticist: To provide guidance on the genetic aspects of the condition and help with family planning and genetic testing.
- Speech Therapist: For children with cleft palate or speech delays, speech therapy can help improve communication skills.

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7. Other Supportive Measures

- Psychosocial Support: The physical and aesthetic challenges associated with Stickler syndrome can sometimes affect emotional well-being. Counselling and support groups can provide emotional and psychological support for affected individuals and their families.
- Regular Monitoring: Individuals with Stickler syndrome should have regular follow-up appointments to monitor the progression of the condition and address new health concerns as they arise.

Did you know?

Stickler Syndrome was first identified in 1965 by American ophthalmologist Gerald Stickler.

Prevalence rates have been estimated at 1-3 per 10,000 births and at 1 per 7,500 births.*

Most investigators believe that the condition is highly under-diagnosed, making it difficult to determine the true prevalence of Stickler syndrome in the general population. Stickler syndrome is one of the most common connective tissue conditions in the United States.

References:

*https://rarediseases.org/rare-diseases/stickler-syndrome/ Accessed 7th March 2025

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- Care packs
- Financial assistance
- Family support coordinator
- Connection to other families