

Stickler Syndrome

Also known as: Stickler dysplasia, hereditary arthro–ophthalmopathy, Weissenbacher–Zweymuller syndrome

Clinical Characteristics

Stickler syndrome is a connective tissue disorder with widely variable expression and no firmly established clinical criteria. The range of symptoms includes ocular findings, hearing impairment, midface underdevelopment, and skeletal findings. Vision problems are usually non-progressive and detectable in newborns. Issues many include myopia, cataracts, glaucoma, retinal detachment, and vitreous abnormalities. Midface hypoplasia is typically seen, as is cleft palate. A small jaw and cleft palate may occur independently, or as part of the Robin sequence. Skeletal abnormalities can include relative short stature, early-onset arthritis, hypermobility, scoliosis and kyphosis, and signs of mild spondyloepiphyseal dysplasia. As many as 50% of patients with Stickler syndrome have mitral valve prolapse. Some patients have bleeding tendencies due to von Willebrand factor.

Stickler Syndrome and Hearing Loss

Hearing loss in Stickler syndrome is primarily due to hypermobility of the middle ear systems. About 40% of individuals with Stickler syndrome have some degree of sensorineural hearing loss, which may or may not be progressive. The degree of severity is variable. Conductive hearing loss can also be seen. There is a high chance of recurrent ear infections, which should be monitored closely.

Natural History

Stickler syndrome is diagnosed in both males and females, and in all ethnicities. The prevalence of the syndrome is estimated to be about 1-3 in 10,000, but no research has yet confirmed this. The condition is most likely under-diagnosed.

Some of the findings common in Stickler syndrome may be present at birth, but it is more likely that most will develop over time. The expression of the syndrome is widely variable, even among affected members of the same family. Myopia is typically congenital, stable, and present in a high degree. Cataracts are often congenital and non-progressive. Some skeletal findings (hypermobility, dysplasia) may manifest early on, but others may not be seen until later (arthritis, short stature, scoliosis/kyphosis). Hypermobility is often lost in the later years. Joint replacement surgery may be needed due to degenerative arthropathy. The onset of hearing loss is usually in childhood, though it can first appear in adolescence or adulthood. With careful monitoring and surveillance, a good prognosis is expected. Intelligence is usually normal. Life expectancy is normal.

Genetics

Three genes have been associated with Stickler syndrome, though mutations in these genes do not account for all cases. *COL2A1* on chromosome 12 encodes a major structural component of collagen type II; 75% of detected mutations causing Stickler syndrome are found in this gene. *COL11A1* and *COL11A2* (found on chromosomes 1 and 6, respectively) encode for components of type IX collagen. Stickler syndrome is **autosomal dominant**. This means that an affected individual has a 50% chance with each pregnancy of having an affected child, and a 50% chance of having an unaffected child. Most individuals with Stickler syndrome inherit the condition from a parent, though some cases are *de novo* (spontaneous).

Management

The diagnosis of Stickler syndrome is made clinically, though the determination of a definitive diagnosis may be somewhat problematic since no clinical criteria currently exist. Genetic testing is available for confirmation of diagnosis, and for prenatal diagnosis if a mutation is identified. Mutations are identified anywhere from 25-80% of the time.

A baseline audiogram should be obtained upon diagnosis. As patients are subject to recurrent ear infections, signs of infection should be carefully looked for and aggressively treated. Myringotomy tubes are often required. Individuals should have biannual audiology evaluations until the age of 5, then annual; changes and progression should be closely monitored. Treatment for hearing loss is usually achieved through amplification, and speech and language therapy.

A baseline ophthalmologic evaluation is also recommended. Regular ophthalmologic assessments (e.g. annually) are indicated. Glasses are often needed. Patients should be instructed to look for warning signs of retinal detachment. Contact sports that could result in detachment should be avoided. A physician with knowledge about vitreoretinal disease should be consulted.

Those with craniofacial issues should be recommended to a comprehensive craniofacial clinic, and at the very least consult an otolaryngologist. Joint issues should be addressed as needed; anti-inflammatory medications and behavior modifications may be the most useful therapies.

Any signs of mitral valve prolapse should prompt a referral to cardiology. A careful history should ask about symptoms such as tachycardia and chest pain.

A scheduled appointment with a geneticist and/or genetic counselor is recommended.

Resources for Families

Statewide Genetics Program

Phone: 608-267-7148

Fax: 608-267-3824

Email: meyeram@dhfs.state.wi.us

Wisconsin First Step Hotline

Phone: 1-800-642-7837 voice/TTY

Website: www.mch-hotlines.org

Wisconsin Bureau for Deaf and Hard of Hearing

Phone: 1-608-266-3118 voice/TTY

Website: www.dhfs.state.wi.us/sensory

Regional Children and Youth with Special Health Care Needs Centers

Centers in Green Bay, Wausau, Milwaukee, Madison, and Chippewa Falls

Website: http://dfhs.wisconsin.gov/DPH_BFCH/cshcn/index.HTM

Parent-to-Parent of Wisconsin

Phone: 1-888-266-0028

Email: mathea@shsmh.org

Family Village online resource

Library Card Catalog of Disorders

www.familyvillage.wisc.edu

Stickler Involved People

www.sticklers.org

National Organization for Rare Disorders (NORD)

www.rarediseases.org