

What are the sulfate transporter-related osteochondrodysplasias?

The sulfate transporter-related osteochondrodysplasias (STROs) are a group of inherited diseases characterized by short stature and short limbs, spine and joint abnormalities, and early-onset osteoarthritis.¹ Individuals with STROs have abnormalities in a protein that transports sulfate into cells, where it is needed for the development of cartilage. The symptoms of an STRO are due to the abnormal formation of cartilage and its conversion to bone.² There are four types of STRO: recessive multiple epiphyseal dysplasia, diastrophic dysplasia, atelosteogenesis type 2 (also known as de la Chapelle dysplasia or McAlister dysplasia), and achondrogenesis type 1B.^{1,3}

What are the symptoms of sulfate transporter-related osteochondrodysplasias and what treatment is available?

Signs and symptoms of the STROs vary in severity, ranging from mild bone abnormalities with joint pain to lethal conditions.⁴ STRO types are distinguished based on clinical and radiological (x-ray) findings.

The mildest STRO type is recessive multiple epiphyseal dysplasia. The majority of individuals are diagnosed in childhood, but some may not be diagnosed until adulthood. Symptoms are variable and may include:⁴

- Mild short stature
- Abnormalities of hands and fingers
- Abnormality of the kneecaps
- Clubfoot (foot turned inward and upward)
- Scoliosis (abnormal curvature of spine)
- Cleft palate (abnormal opening in the roof of the mouth)
- Joint pain, usually beginning in late childhood
- Early-onset arthritis

Symptoms of diastrophic dysplasia are often recognized at birth or during infancy. Some infants have breathing difficulties due to a small rib cage and may require mechanical ventilation. Individuals who survive past infancy typically have a normal life expectancy. Symptoms may include:⁵

- Short stature
- Shortened limbs
- Clubfoot
- Lordosis, kyphosis, and scoliosis (abnormal curvatures of the spine)
- Cleft palate (abnormal opening in the roof of the mouth)
- Early-onset joint pain and joint contractures (tightening of the muscles or tendons preventing full extension)
- Early-onset arthritis

The skeletal findings of atelosteogenesis type 2 resemble those of diastrophic dysplasia, but are more severe. Additional symptoms include a prominent abdomen and distinctive facial features. Affected infants have severe breathing difficulties and do not survive past early infancy.⁶

Achondrogenesis type 1B is the most severe form of an STRO with significant skeletal abnormalities. Some fetuses with achondrogenesis type 1B may have hydrops fetalis (abnormal build-up of fluid in the body) detected by prenatal ultrasound and may not survive the pregnancy. Affected infants have very short limbs, fingers, and toes, a small chest, a prominent abdomen, and die shortly after birth.⁷

There is no cure for the sulfate transporter-related osteochondrodysplasias. Treatment includes supportive care for symptoms. For individuals with recessive multiple epiphyseal dysplasia and diastrophic dysplasia, orthopedic intervention and pain management may be necessary.^{4,5}

How are the sulfate transporter-related osteochondrodysplasias inherited?

The sulfate transporter-related osteochondrodysplasias are autosomal recessive diseases caused by mutations in the *SLC26A2* gene.² An individual who inherits one *SLC26A2* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *SLC26A2* gene mutations, one from each parent, is expected to be affected with one of the sulfate transporter-related osteochondrodysplasias.

If both members of a couple are carriers of a mutation in the same gene, the risk of having an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for the sulfate transporter-related osteochondrodysplasias?

The sulfate transporter-related osteochondrodysplasias can occur in individuals of all races and ethnicities. It is most common in individuals of Finnish ancestry, with a carrier frequency estimated to be 1 in 50.⁸ In the general population, the sulfate transporter-related osteochondrodysplasias are estimated to affect 1 in 100,000 individuals, with a calculated carrier frequency of 1 in 158.⁵

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

Little People of America: www.lpaonline.org

References

1. Karniski, LP. Mutations in the diastrophic dysplasia sulfate transporter (*DTDST*) gene: correlation between sulfate transport activity and chondrodysplasia phenotype. *Hum Mol Genet* 2001; 10(14): 1485-1490.
2. *SLC26A2 Genetics Home Reference*: Available at: <http://ghr.nlm.nih.gov/gene/SLC26A2> Accessed on: March 23, 2012.
3. *Atelosteogenesis type 2. Genetics Home Reference*. Available at: <http://ghr.nlm.nih.gov/condition/atelosteogenesis-type-2> Accessed June 11, 2012.
4. Bonafe L *et al.* Multiple Epiphyseal Dysplasia, Recessive. *Gene Reviews* Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1306/> Accessed March 26, 2012
5. Bonafe L *et al.* Diastrophic Dysplasia *GeneReviews* Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1350/#diastrophic-d.grID94412> Accessed March 23, 2012
6. Bonafe L *et al.* Atelosteogenesis Type 2 *GeneReviews* Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1317/> Accessed March 26, 2012
7. Bonafe L *et al.* Recessive Achondrogenesis Type 1B *Gene Reviews* Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1516/> Accessed March 26, 2012
8. Hastbacka J *et al.* Identification of the Finnish founder mutation for diastrophic dysplasia (DTD). *Eur J Hum Genet* 1999; 7; 664-670.