

Genetic Testing for Loeys-Dietz Syndrome (LDS)

What is Loeys-Dietz Syndrome?

Loeys-Dietz Syndrome is an inherited disease that can lead to rupture of the body's main blood vessels.

Loeys-Dietz Syndrome (LDS) is an inherited connective tissue disorder that affects the cardiovascular system (heart and blood vessels) as well as the skeletal system (bone structures) and the skin. Individuals with LDS may have loose joints, very long fingers and toes, very wide-set eyes, a little flap of tissue hanging down at the back of their mouth (bifid uvula), a sideways curved spine (scoliosis), and/or velvety, translucent skin that bruises easily. The most dangerous consequences of LDS, however, are less obvious from the outside. LDS often leads to weak spots (aneurysms) in the arteries, the blood vessels carrying blood from the heart to the rest of the body. If left untreated, these weak spots will become bigger due to stretching (dilation), and some will eventually split lengthwise along the artery wall (dissect) or rupture, potentially leading to death. Luckily, this devastating outcome can often be prevented through timely treatment and preventative surgery.

How is Loeys-Dietz Syndrome treated?

Loeys-Dietz Syndrome is treated with medication and preventative surgery.

The worsening of aneurysms can be slowed through drug treatment, and aortic dissection or rupture can be prevented by surgically replacing the dilated part of the aorta before it dissects or ruptures. In addition, individuals with LDS can make some precautionary lifestyle adjustments. They should avoid contact sports, competitive sports, and isometric exercises (exercises that involve tightening a muscle without moving), or frequent use of decongestants, all of which increase the risk of aortic rupture. In some individuals with LDS, activities that involve breathing against resistance, such as scuba diving or playing a wind instrument, are also not advised since these can lead to episodes of spontaneous lung collapse (pneumothorax).

What causes Loeys-Dietz Syndrome?

*Loeys-Dietz Syndrome is caused by variations in the genes *TGFBR1* or *TGFBR2*.*

Most or all cases of LDS are due to a genetic defect in either the gene *TGFBR1* or the gene *TGFBR2*. If an individual harbors an LDS-associated genetic defect in one of these genes, each of his or her children has a 50% chance of inheriting this defect and, thus, the condition.

How is Loeys-Dietz Syndrome diagnosed?

Loeys-Dietz Syndrome is usually diagnosed based on the presence of a characteristic combination of several different symptoms.

Two different types of Loeys-Dietz Syndrome are recognized, LDS type 1 and LDS type 2. Each type shares many symptoms with another, more common inherited disease. LDS₁ looks a lot like Marfan Syndrome, and LDS₂ like vascular Ehlers-Danlos Syndrome. It is very important to determine if a patient suffers from LDS, Marfan Syndrome, or vascular Ehlers-Danlos Syndrome, because the treatment recommendations for these three diseases differ. Aneurysms associated with LDS grow faster than the aneurysms seen in Marfan patients and require surgical repair at a younger age to avoid dissection and rupture. On the other hand, prophylactic surgical repair is not recommended for vascular Ehlers-Danlos patients, because it tends to cause more damage than it does good in these patients.



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How can genetic testing help individuals and families with Loeys-Dietz Syndrome?

Genetic testing can help to distinguish Loeys-Dietz Syndrome from Marfan Syndrome and vascular Ehlers-Danlos Syndrome.

If the familial mutation is known, genetic testing can help to identify family members who are at risk of developing Loeys-Dietz Syndrome and should take preventative measures. Testing for the familial mutation can also help to identify family members who are not at highly increased risk of Loeys-Dietz Syndrome.

Often, but not always, LDS can be distinguished from Marfan Syndrome based on the presence or absence of some characteristic signs. For example, the flap of tissue hanging down at the back of the mouth only occurs in LDS patients and not in Marfan patients. On the other hand, Marfan patients, but not LDS patients, often have the lens displaced in one or both of their eyes. However, such characteristic signs of one or the other disease are not always present, making it sometimes difficult to tell LDS and Marfan patients apart. It's even more difficult to distinguish LDS and vascular Ehlers-Danlos Syndrome, which both present with velvety and translucent skin that bruises easily. Since all three diseases are caused by mutations in different genes, genetic testing can help to tell them apart. Once the specific mutation affecting an extended family (the familial mutation) has been identified, genetic testing can also help to determine who in the family carries the familial mutation and is therefore at high risk of LDS, even if they do not show symptoms yet, and who does not carry the familial mutation and is therefore at much lower risk of LDS.

If you still have questions about Loeys-Dietz Syndrome, please contact us or consult any of the other resources listed below:

Correlagen Diagnostics
www.correlagen.com
phone: 1-866-647-0735

Loeys-Dietz Syndrome Foundation
<http://www.loeysdietz.org>
email: info@loeysdietz.org

National Marfan Foundation (NMF)
www.marfan.org
phone: 1-800-862-7326 staff@marfan.org
email: staff@marfan.org

National Institute of Arthritis and Musculoskeletal and Skin Diseases
http://www.niams.nih.gov/Health_Info/Marfan_Syndrome/default.asp

Additional Reading:

Loeys, BL, Dietz HC. GeneReviews, <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=loeys-dietz>



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