Loeys Dietz syndrome is a genetic condition that affects connective tissue. Connective tissue is a type of tissue that helps to hold everything together, like a glue for your body. The main body systems affected by Loeys Dietz syndrome include cardiovascular, skeletal, cutaneous (skin), and ocular (eyes):

- Cardiovascular – The most common cardiac findings associated with Loeys Dietz syndrome are congenital (from birth) heart defects, such as patent ductus arteriosus (PDA), atrial or ventricular septal defects (ASD/VSD), and bicuspid aortic valve (BAV).
- Skeletal – Patients with Loeys Dietz syndrome can have long fingers and toes, scoliosis, joint laxity, chest wall deformities (pectus excavatum or pectus carinatum, and/or osteoarthritis, as well as craniofacial findings such as flat cheek bones, downward-slanting eyes, craniosynostosis, cleft palate, and chin deformities (such as a small, receding chin).
- Cutaneous – Skin findings associated with Loeys Dietz syndrome include soft, velvety, translucent skin, easy bruising, abnormal scarring, and hernias.
- Ocular – Eye issues seen in patients with Loeys Dietz syndrome include myopia (nearsightedness), eye muscle disorders, and retinal detachment.

Additional unique clinical findings include arterial tortuosity (twisting arteries), hypertelorism (widely spaced eyes), bifid or broad uvula, and aortic aneurysms and dissections. Both aortic aneurysms and dissections can be life threatening. Some patients with Loeys Dietz syndrome also have food allergies, asthma, eczema, esophagitis/gastritis, and/or inflammatory bowel disease.

There are five types of Loeys Dietz syndrome which are associated with changes in different genes: I (*TGFBR1)*, II (*TGFBR2)*, III (*SMAD3*), IV (*TGFB2*), and V (*TGFB3*). Loeys Dietz syndrome can range greatly in severity, and there can be much variability even between affected members of the same family. Individuals may have few or no symptoms while others may have severe and early-onset health concerns.

Causes

Loeys Dietz syndrome is caused by pathogenic variants in the *TGFBR1*, *TGFBR2*, *SMAD3*, *TGFB2*, or *TGFB3* genes, which are inherited in an autosomal dominant pattern. This means that a single copy of the pathogenic variant is enough to cause an individual to develop the condition, and anyone who carries the pathogenic variant has a 50% chance to pass it down to any children they have. About 25% of people who have Loeys Dietz syndrome have a

parent who also has it. The other 75% are the first ones in their family to have it (called *de novo*).

Diagnosing Loeys Dietz syndrome

While genetic testing for Loeys Dietz syndrome can be helpful, medical providers may use other pieces of information, such as a physical exam and family history, to help establish the diagnosis. Some red flags that can increase the chance for Loeys Dietz syndrome in a family include:

- Aortic root enlargement or dissection
- Arterial tortuosity in the head and neck vessels
- Aneurysms
- Characteristic craniofacial, skeletal, cutaneous, and vascular features
- Family history of health concerns related to Loeys Dietz syndrome, or a family history of a pathogenic variant in the *TGFBR2*, *SMAD3*, *TGFB2*, or *TGFB3* genes.

Due to the varying types of genetic changes that have been reported in the *TGFBR1*, *TGFBR2*, *SMAD3*, *TGFB2*, or *TGFB3* genes in association with Loeys Dietz syndrome, genetic testing for Loeys Dietz syndrome involves sequence and deletion/duplication analysis. About 90-95% of those who meet the criteria for Loeys Dietz syndrome based on their personal and family history will have a pathogenic variant in one of the known causative genes. This also means that some individuals who appear to have Loeys Dietz syndrome will have negative genetic test results.

Medical Management for Loeys Dietz syndrome

Treatment for Loeys Dietz syndrome can sometimes vary depending on the individual person and their specific health concerns and should be discussed with a medical provider who is familiar with Loeys Dietz syndrome. Management for Loeys Dietz syndrome is generally focused on monitoring for the potential health complications. Individuals with Loeys Dietz syndrome are recommended to have regular eye exams by an ophthalmologist, annual cardiac imaging to monitor the aorta (screening may be more frequent if dilation is found), and intervention and follow-up by an orthopedist for those with progressive scoliosis or other skeletal problems. Additional screening may be recommended depending on the individual's personal and family history. Because of the cardiovascular and other risks, it is often suggested that individuals with Loey Dietz syndrome avoid certain activities such as contact and competitive sports. It is also important for women with Loeys Dietz syndrome who are considering pregnancy to discuss options and review these risks beforehand when

possible.

Click here to learn more about scheduling a genetic counseling appointment for questions about pediatric or adult genetic conditions.

Resources

Loeys Dietz Syndrome Foundation

MedlinePlus Genetics