Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate discussion between a provider and their patient.

Genetic Insights test results: **Loeys-Dietz syndrome**

Key results

A pathogenic or likely pathogenic variant associated with Loeys-Dietz syndrome (LDS) was found in the *TGFBR1* gene.

People with LDS have a significantly increased risk of developing an aortic aneurysm and/or dissection and may have other health concerns.

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and not intended for diagnosis. A follow-up genetic test should be performed in a clinical setting before any other action is taken.	**Ready to order?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Blueprint Genetics® offers LDS testing. To confirm this test result, **targeted variant testing** for the variant identified is available. You can order a confirmation test here: Blueprint Genetics/TVT **Have questions?** Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results.
Refer your patient to a genetic counselor. *Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.*	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Connective Tissue Disorder Report at no additional cost. To find a genetic counselor with expertise in connective tissue disorder genetics practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org

Patient conversation starters:

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. The next step is to have your result confirmed with a second genetic test.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your online Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.

What is LDS?

LDS is a hereditary connective tissue disorder characterized by vascular, skeletal, craniofacial, and cutaneous findings.[1,2]

People with LDS are at a significantly increased risk of developing an aneurysm, dissection, and/or rupture of the aorta or along the arterial tree.[1,2]

Arterial aneurysms are often asymptomatic, and individuals may first present with an acute aortic dissection with high morbidity and mortality.[2,3]

There is clinical variability between individuals with LDS.[1] Features outside of vascular involvement may include scoliosis, joint laxity, cleft palate, easy bruising of the skin, and allergic diseases.[1,2]

Diagnosis is typically made by a specialist, such as a medical geneticist, and management is best coordinated by a multidisciplinary care team.[1]

See the Management options section for more detail.

Patient conversation starters:

Loeys-Dietz syndrome (or LDS) is caused by having a DNA variant in a certain gene.

LDS is a connective tissue disorder; that means the tissues that help connect our bodies together—like the blood vessels—can be affected.

People with LDS have a higher than typical chance of having a tear in a major blood vessel like the aorta. But not everyone with LDS will have a tear in a blood vessel.

People with LDS should see a specialist, including a geneticist, to help monitor for and prevent health issues.

What this result means for family members

There are 2 primary ways someone can have a DNA variant associated with LDS:

The DNA variant can be inherited from a biological parent. In this case, at least 1 parent has the same DNA variant. Each full sibling and each child of someone with the variant has a 50% chance of having the same variant.

The DNA variant can arise in someone for the first time (also called a de novo variant). In this case, their children have a 50% chance of having the variant. Neither biological parent nor any siblings are likely to have the variant.

In people with a confirmed DNA variant associated with LDS, genetic testing for family members may help inform their risks and screening protocols.[3] Therefore, it is strongly recommended that individuals share these results with their biological relatives.

Patient conversation starters:

There are 2 ways someone can end up having a DNA variant linked to LDS.

- First, it can be passed down from a parent. In this case, 1 parent would have that same DNA variant. Siblings would have a 50% chance (1 in 2 chance) of having the DNA variant
- Second, it is possible that the DNA variant happens in someone in a family for the first time. In this case, parents and siblings are not likely to have the DNA variant

However, in either case, each child of someone with a DNA variant linked to LDS has a 50% chance of having the same DNA variant.

Sharing this result with your family members is important so they can talk to a healthcare provider about genetic testing for LDS.

Management options

There are management and treatment options for people with LDS. Select clinical guidelines from the American College of Cardiology Foundation/American Heart Association[3] include:

Scenario	Option(s)
Screening	People with a confirmed genetic variant associated with LDS should undergo complete aortic imaging at initial diagnosis and 6 months thereafter to establish if enlargement is occurring, and yearly magnetic resonance imaging of the cerebrovascular circulation to the pelvis
Surgical aneurysm repair	Surgical repair of the aorta in all adult patients with LDS should be considered at an aortic diameter based on clinical guidelines
Control of hypertension	Stringent control of hypertension, some exercise restrictions, and other risk-reducing measures may be recommended
Pregnancy	Individuals considering pregnancy should be counseled about the risks. Optimal care includes involvement with a high-risk maternal-fetal team along with an aortic specialty team[3]

Patient conversation starters:

It's recommended that people with LDS make a plan to monitor their health. This way, any health problems can be found as early as possible, and a treatment plan can be made.

If your genetic test result is confirmed, it's important to work with the right specialists, including a geneticist, to make a plan that's right for you.

See the American College of Cardiology Foundation/American Heart Association[3] and expert reviewed clinical guidelines[1] for complete recommendations. Guidelines and recommendations may change over time.

If this result is confirmed, a medical geneticist should be consulted for further clinical management. To locate a genetics center, please visit the American College of Medical Genetics and Genomics.

Additional resources

The following advocacy groups have additional information and resources about LDS:

Loeys-Dietz Syndrome Foundation: LoeysDietz.org
John Ritter Foundation: JohnRitterFoundation.org

References

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2. Loeys B and Dietz H. Loeys-Dietz Syndrome. February 28, 2008. Updated March 1, 2018. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2022. https://www.ncbi.nlm.nih.gov/books/NBK1133/
3. Hiratzka LF, Bakris GL, et al. ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. *Circulation.* 2010;121(13):e266-369. doi:10.1161/CIR.0b013e3181d4739e