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: **Vascular Ehlers-Danlos syndrome**

Key results

A pathogenic or likely pathogenic DNA variant associated with vascular Ehlers-Danlos syndrome (vascular EDS) was found in the *COL3A1* gene.

People with vascular EDS have a significantly increased risk of developing an aortic aneurysm, dissection and/or rupture, rupture of certain organs, and 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 vascular EDS 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 vascular EDS?

Vascular EDS is a hereditary connective tissue disorder characterized by arterial, intestinal, and uterine fragility and rupture.[1,2] It is the result of a pathogenic or likely pathogenic DNA variant in the *COL3A1* gene.

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

There is clinical variability between individuals with vascular EDS.[1,2]

Features outside of vascular involvement may include rupture of hollow organs such as the intestines or uterus during pregnancy, pneumothorax, and translucent skin with easy bruising.[1,2]

Diagnosis is typically made by a specialist such as a medical geneticist. Management is complex and best coordinated by a multidisciplinary care team.[1,2]

See the Management options section for more detail.

Patient conversation starters:

Vascular EDS is a connective tissue disorder; that means the tissues that help connect our bodies together—like the blood vessels and skin—can be affected. It is caused by having a DNA variant in a certain gene.

People with vascular EDS have a higher than typical chance of having a tear in a major blood vessel like the aorta.

There is also a higher chance that some organs, like the intestines, can tear. But not everyone with vascular EDS will have these problems.

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

What this result means for family members

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

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 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 vascular EDS, 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:

Vascular EDS is caused by having a DNA variant in a certain gene.

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

- 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 arises 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 vascular EDS has a 50% chance of having the same DNA variant.

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

Management options

There are management and treatment options for people with vascular EDS. Vascular management often follows the American College of Cardiology Foundation/American Heart Association guidelines and comprehensive vascular Ehlers-Danlos clinical guidelines have been extensively reviewed by experts.[2,3] Select guidelines include:

Scenario	Option(s)
Monitoring and screening	To reduce the risk of arterial dissection or rupture, noninvasive imaging to screen for aneurysms with prophylactic aneurysm repair may be considered, although this should be weighed against the risks related to tissue fragility[2,3]
Additional risk reduction	Maintenance of blood pressure in normal to low ranges is critical[2] Avoidance of contact sports or isometric exercise is encouraged[2]
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[2,3]

Patient conversation starters:

It's recommended that people with vascular EDS 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[2] 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 vascular EDS:

The Ehlers-Danlos Society: Ehlers-Danlos.com
The VEDS Movement: TheVEDSMovement.org
John Ritter Foundation: JohnRitterFoundation.org

References

1. Byers PH. Vascular Ehlers-Danlos Syndrome. September 2, 1999. Updated February 11, 2019. 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/NBK1494/
2. Byers PH, Belmont J, Black J, et al. Diagnosis, natural history, and management in vascular Ehlers-Danlos syndrome. *Am J Med Genet C Semin Med Genet*. 2017;175(1):40-47. doi:10.1002/ajmg.c.31553
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

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