Genetic Insights: quick reference guide for healthcare providers

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

Genetic Insights test results: **Classical Ehlers-Danlos syndrome**

Key results

A pathogenic, or likely pathogenic, variant associated with classical Ehlers-Danlos syndrome (EDS) was found in the *COL5A1* gene.

People with classical EDS generally have joint hypermobility, skin hyperextensibility, and abnormal scarring.

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and is 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 classical 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.	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.
Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.	To find a genetic counselor with expertise in connective tissue disorders 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 classical EDS?

Classical EDS is a hereditary connective tissue disorder mainly characterized by skin hyperextensibility, abnormal wound healing, and joint hypermobility.[1,3]

People with classical EDS may also have an increased risk for mitral valve prolapse and, less frequently, tricuspid valve prolapse. Aortic root dilatation has been reported, but rarely progresses.[1,3]

Skin hyperextensibility is one of the major features of classical EDS. The severity of other features such as joint hypermobility depends on other factors such as age, gender, and ethnic background.[1,3]

Diagnosis is typically made by a specialist such as a medical geneticist and includes a clinical evaluation and review of family history.

Management is best coordinated by a multidisciplinary care team with a specific focus on the skin and joints [1,2]

See the Management options section for more detail.

Patient conversation starters:

Classical Ehlers-Danlos syndrome (or classical EDS for short) is caused by a DNA variant in a certain gene.

Classical EDS is a connective tissue disorder. That means the tissues that help connect our bodies together—like the blood vessels and bones—can be affected.

People with classical EDS have a higher than typical chance of having problems with their skin or joints.

It is best for people with classical EDS to see a specialist to help monitor and prevent health issues.

What this result means for family members

There are 2 primary ways someone can have a DNA variant associated with Classical 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 it
- The DNA variant can arise in someone for the first time (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 classical EDS, genetic testing for family members may help inform their risks and screening protocols.[3]

A genetic counselor can help determine the most appropriate testing options. Therefore, it is strongly recommended that people share their results with their biological relatives.

Patient conversation starters:

Classical EDS can run in families.

The DNA variants that cause classical EDS can be inherited or passed down from parents to their children. In this case, full siblings would have a 50% (or 1 in 2) chance of having the same DNA variant. Other relatives might also have the same DNA variant.

It is also possible that the DNA variant happens in someone in a family for the first time. In this case, your 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 classical EDS 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 classical EDS.

Management options

There are management and treatment options for people with classical EDS. Clinical recommendations have been published by several expert groups.[1-3] Select recommendations from The International Consortium on the Ehlers–Danlos syndromes expert review include[1]:

Scenario	Option(s)
General screening	People with a confirmed genetic variant associated with classical EDS should follow up with a specialist, such as a medical geneticist, regarding appropriate surveillance and prevention of primary manifestations with a specific focus on the skin and joints Evaluation includes an echocardiogram for aortic root dilation and mitral valve prolapse. However, ongoing surveillance frequency should be determined by results and other clinical history
Cutaneous conditions	Avoid unnecessary trauma (damage) to the skin Any wounds should be treated by an expert Consider medications or supplements that may assist in wound healing and/or reducing bleeding time
Musculoskeletal conditions	Physiotherapy may be beneficial for hypotonia or developmental delays Avoid certain competitive physical activities that may cause undue joint stress Joint hypermobility should be managed by experts Supportive devices and pain management should be discussed and implemented on an individual basis
Pregnancy	Optimal care includes involvement with a high-risk maternal-fetal team who will carefully monitor the pregnancy; this is especially important as risk of premature membrane rupture may be high

Patient conversation starters:

It's recommended that people with classical 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—like a geneticist—to make a plan that's right for you.

Recommendations may change over time.

If this result is confirmed, a specialist should be consulted for further clinical management. To locate a genetics center or specialty clinic, please visit the American College of Medical Genetics and Genomics at www.acmg.net/ACMG/Genetic_Services_Directory_Search.aspx

Additional resources

The following patient advocacy groups have additional information and resources about classical EDS:

The Ehlers-Danlos Society: Ehlers-Danlos.org

References

1. Bowen JM, Sobey GJ, Burrows NP, et al. Ehlers–Danlos syndrome, classical type. *Am J Med Genet Part C Semin Med Genet*. 2017;175(1):27-39. doi:10.1002/ajmg.c.31548
2. Malfait F, Wenstrup R, De Paepe A. Classic Ehlers-Danlos Syndrome. May 29, 2007. Updated July 26, 2018. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. University of Washington, Seattle; 1993-2022. https://pubmed.ncbi.nlm.nih.gov/20301422
3. Malfait F, Wenstrup RJ, De Paepe A. Clinical and genetic aspects of Ehlers-Danlos syndrome, classic type. *Genet Med*. 2010;12(10):597-605. doi:10.1097/GIM.0b013e3181eed412