Evaluation for Ehlers-Danlos syndrome: referral criteria

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Clinical question
Which patients with hypermobility or other symptoms suggestive of Ehlers-Danlos Syndrome (EDS) should be referred to Genetics for evaluation?

Recommendations
EDS is a group of rarely occurring, heritable connective tissue disorders characterized by fragile and hyperextensible skin, delayed wound healing with formation of atrophic scars, easy bruising, and generalized joint hypermobility. Given its rarity, patients with suspected EDS should be screened prior to Genetics referral, using the following criteria:

From clinical exam (patient must meet all these criteria):
- Passive dorsiflexion of each fifth finger greater than 90°
- Passive apposition of each thumb to the flexor surface of the forearm
- Hyperextension of each elbow greater than 10°
- Hyperextension of each knee greater than 10°
- Ability to place the palms flat on the floor with the knees fully extended

From clinical and family history (patient must meet at least one of these criteria):
- Personal or family history of rupture of vessels or hollow organs
- Personal or family history of aortic root dilatation
- Personal or family history of vascular or classic EDS, identified either by molecular genetic testing or clinical diagnosis by a geneticist

How could this change my practice?
The newly established set of criteria must be met before placing a Genetics referral for the evaluation of EDS. For all patients, accurate screening and evaluation allows for accurate diagnosis, patient education, and management.

Why did we choose this topic?
Kaiser Permanente Washington’s Genetics Department has noted an increase in referrals for evaluation of EDS, from about 1 every 2 months to 10–15 per month. Patients with chronic pain who want to identify the cause and potential treatments for their pain have accounted for much of the increase, by either physician or self-referral. However, the vast majority of patients we see for evaluation of EDS do not meet the diagnostic criteria. The high volume of EDS evaluations has also limited access to Genetics services for other indications.

Avoiding unnecessary referrals and evaluations is part of providing high-quality, patient-centered, evidence-based health care. By screening patients with suspected EDS prior to Genetics referral, we can minimize unneeded evaluations, improve patient satisfaction, and use our resources more effectively.

More about Ehlers-Danlos syndrome
Currently, EDS is classified into six major types:
Classical (EDS types I and II) occurs in approximately 1 in 20,000-40,000 people worldwide. Diagnosis is based on clinical findings and confirmed by identification of a heterozygous pathogenic mutation in either the COL5A1 or the COL5A2 genes.

Hypermobility (EDS type III) occurs in approximately 1 in 15,000 people. Diagnosis is based on clinical findings and confirmed by identification of a heterozygous pathogenic mutation in the COL3A1 gene.

Vascular (EDS type IV) occurs in approximately 1 in 250,000 people.

Kyphoscoliosis (type VIA), arthrochalasia (types VIIB and VIIIB), and dermatosparaxis (type VIIIC) together total fewer than diagnoses 200 worldwide.

Given the rarity of all forms of EDS, patients should be screened prior to Genetics referral. For all patients, accurate screening and evaluation allows for accurate diagnosis, patient education, and management.

Resource

References
