Ehlers-Danlos Syndrome

Dr. Jon M. Trister MD
Dr. Renata Trister DO
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What is Ehlers-Danlos Syndrome?

• Ehlers–Danlos syndrome (EDS) (also known as Cutis hyperelastica) is a group of inherited connective tissue disorders, caused by a defect in the synthesis of collagen (Type I, III, or V). The collagen in connective tissue helps tissues resist deformation.

• The syndrome is named after two physicians, Edvard Ehlers from Denmark, and Henri-Alexandre Danlos from France, who identified it at the turn of the 20th century.

• EDS is known to affect men and women of all racial and ethnic backgrounds.

• Over 1 million people in US have EDS
Connective Tissue Disorders and Ehlers-Danlos Syndrome

- Collagen is the most abundant protein in the human body. It provides structural strength in human tissues, including heart and blood vessels, eyes and skin, cartilage and bone. When muscles, ligaments, tendons and even large organs are built with structurally defective collagen, there can be systemic weakness and instability evident throughout. Connective tissue disorders such as Ehlers-Danlos syndrome cause multiple manifestations that affect many functions of the human body.

Types, Genotypes and Phenotypes

- **Currently** there are six distinct types of EDS currently identified. All share joint laxity, soft skin, easy bruising, and some systemic manifestations. Each type is thought to involve a unique defect in connective tissue, although not all of the genes responsible for causing EDS have been found.
- The types may appear clear and defined, but EDS (as most other illnesses) rarely permits easy classification. Although the type almost always runs true within each family, the symptoms of individual family members can vary so widely from each other that EDS is either misdiagnosed or ignored, and therefore is probably more frequent than previously thought. Current research estimates incidence at one in 2,500 to 5,000.
• A wide spectrum of physiological reactions, to an inherited collagen defect, expressed uniquely in each individual.
• Although the same genetic fault is inherited in a family, each person develops unique ways of handling EDS.
• This can cause symptoms and fragility throughout the body.

EDS Classifications:

The collagen fibril and EDS. (a) Normal collagen fibrils are of uniform size and spacing. Fibrils from a patient with dermatosparaxis (b) show dramatic alterations in fibril morphology with severe effects on tensile strength of connective tissues. Patients with classical EDS (c) show composite fibrils. Fibrils from a TNX-deficient patient (d) are uniform in size and no composite fibrils are seen. TNX-null (e) fibrils are less densely packed and not as well aligned to neighboring fibrils.
Types, Genotypes and Phenotypes

1) Hypermobility

- Most common type, distinctive cause unidentified.
- Soft skin, Generalized joint hypermobility, skin involvement (including possible hyperextensibility or smooth skin), chronic joint pain, recurrent joint dislocations
- Joint laxity, easy bruising
- To date, no distinctive biochemical collagen finding has been identified by researchers. Inherited in an autosomal dominant manner.

2) Classical

[COL5A1 & COL5A2]:

- Variable skin hyperextensibility, widened atrophic scars (tissue fragility), joint hypermobility, easy bruising; Occasional internal organ fragility
- Joint laxity, easy bruising
- Soft, fragile, elastic skin
- In some families type V collagen is affected (abnormal electrophoretic mobility of proα1(V) or proα2(V) chains) as well as type I. Inherited in an autosomal dominant or recessive manner.
Types, Genotypes and Phenotypes

3) Vascular

- Fragility of arteries, intestines & other internal organs
- Soft, fragile, elastic, translucent skin
- Joint laxity, easy bruising
- Caused by structural defects in the proα1(III) chain of collagen type III, encoded by the COL3A1 gene. Inherited in an autosomal dominant manner. VEDS incidence is estimated at one in 250,000; particularly serious because of possible arterial or organ rupture.
- Arterial/intestinal/uterine fragility or rupture, extensive bruising, hypermobility of small joints, early onset varicose veins, and pneumothorax.

4) Kyphoscoliosis

- Very rare; kyphoscoliosis, hypotonia, fragility of eyes and arteries
- Soft, fragile, elastic skin
- Joint laxity, easy bruising
- Result of a deficiency of lysyl hydroxylase (procollagen-lysine 5-dioxygenase, or PLOD), which is a collagen-modifying enzyme. Inherited in an autosomal recessive manner. Can be diagnosed through urine test.
Types, Genotypes and Phenotypes

5) Arthrochalasia

• Very rare
• Extreme joint laxity, easy bruising
• Soft, extremely fragile skin, atrophic scars
• Osteopenia
• Caused by mutations leading to deficient processing of the amino-terminal end of proα1(I) [type A] or proα2(I)[type B] chains of collagen type I. Inherited in an autosomal dominant manner. Can also be diagnosed by skin biopsy.

6) Dermatosparaxis

• Very rare
• Severe skin fragility, sagging redundant skin; ± soft doughy skin texture, easy bruising, premature rupture of fetal membranes, and large hernias (umbilical and inguinal).
• Joint laxity, easy bruising
• Caused by a deficiency of procollagen I N-terminal peptidase. Inherited in an autosomal recessive manner. Can be diagnosed by skin biopsy.
EDS

• All types of EDS include some degree of joint hypermobility, resulting in:
  • Pain - chronic and widespread
  • Joint instability
  • Spontaneous subluxations/dislocations.

Treatment

• EDS itself is not curable, but many of its effects and symptoms are treatable. So an EDS diagnosis is not really an answer — it is just the first question.
Prolotherapy

Definition

Indications

Contraindications

Frequency of treatments

When do you need imaging guidance. Do you?

When to stop treatment? Prophylactic Prolo?

Other treatments during prolotherapy: neural, mesotherapy, neuro-prolo, Physical therapy; OMT-manual therapy; Pharmacological; Supplements.

History and physical examination. Detailed. Very important.

Review diagnostic tests: Imaging; Labs

Review current medications. Allergy to local anesthetics and fish oil

Communicating with referring physician

Consent for treatment. Discuss procedure, side effect and possible complications in details. Give patient written instruction and time to study. Encourage to call if any questions. Avoid treatment during first treatment unless certain circumstances

Discuss cost and insurance non-coverage. Avoid negotiation

Scheduling visit: Day of the week; Time. Driving home. Food.
Infectious diseases

Communication with referring physician

NSAID Antiplatelets Coumadin

Heart murmur. Antibiotics prophylaxis.

Presence of immunocompromised illnesses;

Special consideration

Morning before treatment: Food

Premedication

Selection of solution

Prolotherapy: Post procedure

Driving home

Pharmacological management: Opioids; cold/heat;

Exercises: when and how much?

Follow up

Complications

Hematomas
Nerve damage
Vascular damage
Hemarthrosis
Allergic reactions
Side effect to medications
Bleeding
Infection

Solutions

Dextrose
Sodium Morrhuate
P2G
PRP
Autologous blood
Stem cells (non-embryonic, mesenchimal)