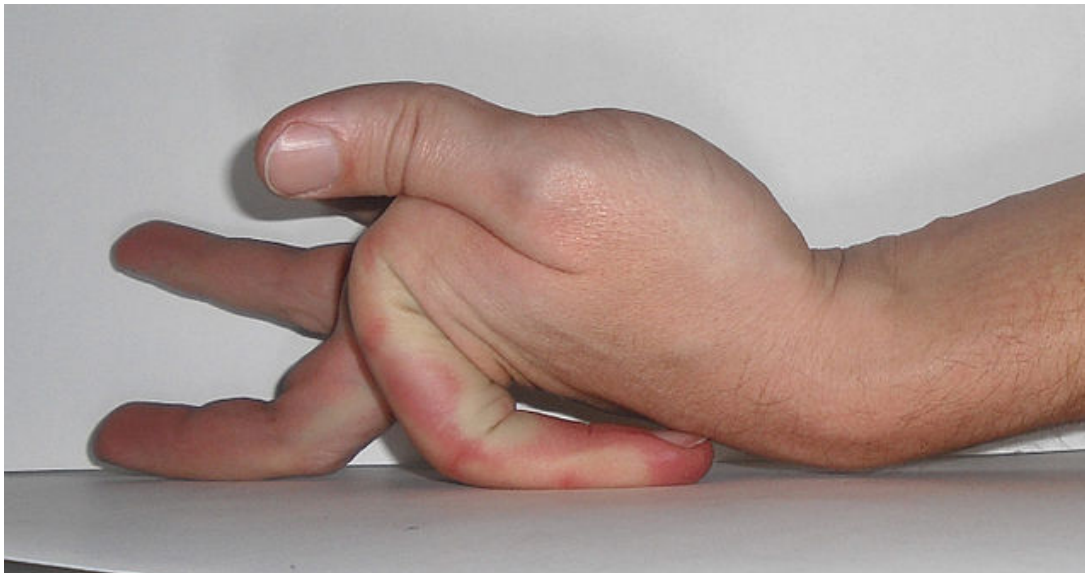


Ehlers-Danlos Syndrome (EDS, Elastic Skin) — Causes and Symptoms

[See online here](#)

EDS — a clinically heterogeneous syndrome involving a genetic defect in connective tissue structure and synthesis, specifically collagen that affects joints, skin and blood vessels, is a group of inherited disorders characterized by stretchy, fragile skin and extremely flexible joints. An even severe form of the disease involves the blood vessels and is called vascular Ehlers-Danlos syndrome. Prognosis is clearly guided by the type of EDS, however, there is no cure for the disease.



Definition of EDS

Ehlers-Danlos syndrome as a genetic defect

EDS is a term used for a **group of different inherited disorders** having a single **genetic defect**—in collagen and [connective tissue](#)—common between them. Connective tissue is a mixture of proteins and other substances that provide the underlying structures with elasticity and strength.

People suffering from EDS have:

- Articular hypermobility
- [Skin](#) extensibility
- Tissue fragility
- Vascular EDS patients have [blood vessels](#) that are prone to rupture (especially of the intestine and uterus)

Epidemiology of EDS

While mild or incomplete forms are more common but undiagnosed, the prevalence of EDS is 1 in 5.000 people. It is often diagnosed in childhood and has no racial predominance. Also, it exists equally in both sexes as the differing phenotypes are located on **autosomes** and not sex chromosomes. Type IV EDS patients have a shortened lifespan as compared to other types.

Etiology of EDS

Ehlers-Danlos syndrome caused by gene mutations

More than a dozen gene mutations have been found in association with EDS. The classical type of disease is a consequence of mutation in either **COL5A1 or COL5A2 gene**. The genes involved are responsible for the synthesis of various types of collagen. Other gene mutations include:

- TNXB (small percentage in hypermobility type)
- COL3A1 (vascular type)
- PLODA1 (kyphoscoliosis type)
- COL1A1, COL1A2 (arthrochalasia type)
- ADAMTS2 (dermatosparaxis)

Pathophysiology of EDS

The inherited group of disorders is a consequence of various **abnormalities in synthesis and metabolism of collagen** as well as other connective tissue proteins like Proteoglycans, elastin and macromolecular proteins. These abnormalities manifest as a result of defects in:

- Elasticity
- Inherent strength
- Integrity
- Healing properties of tissue

Collagen - the most abundant protein is a product of 29 genes on 15 different chromosomes that code for 19 identifiable forms of collagen molecules. Various gene mutations result in a defective piece of collagen, eventually leading to EDS.

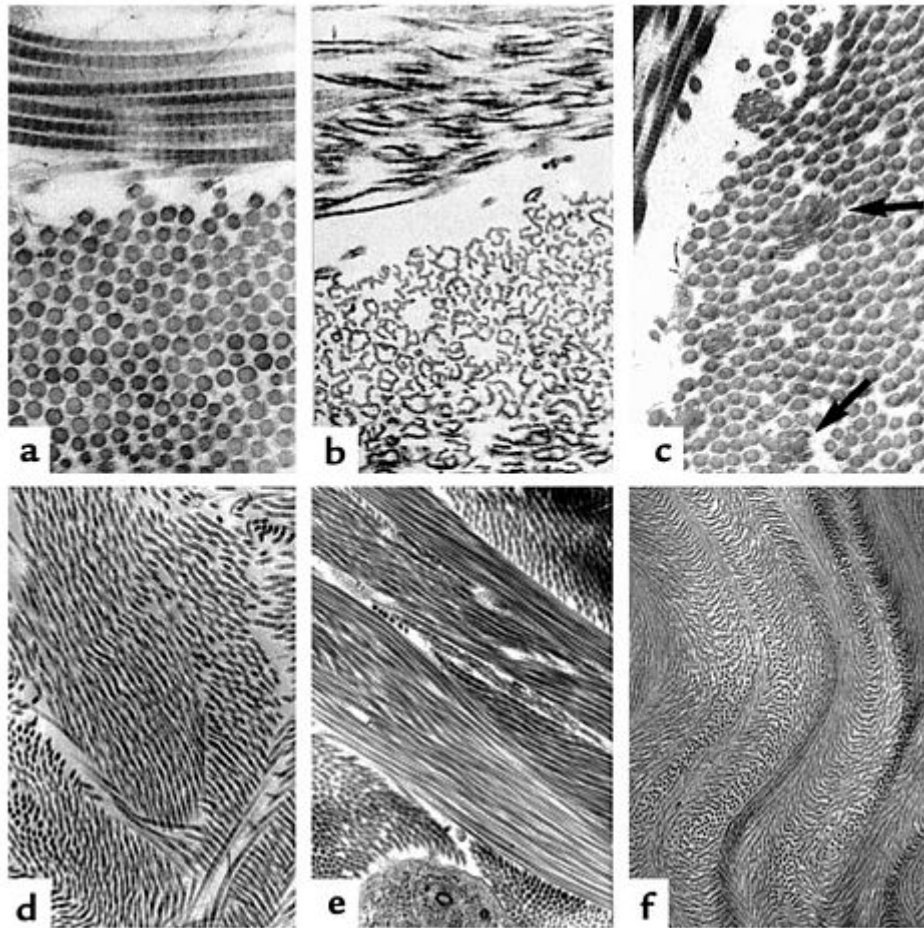


Image: "The collagen fibril and EDS. (a) Normal collagen fibrils are of uniform size and spacing. Fibrils from a patient with dermatosparaxis (b) show dramatic alterations in fibril morphology with severe effects on tensile strength of connective tissues. Fibrils from a patient with classical EDS (c) may show composite fibrils (arrows). 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." by JohnGohn. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Symptoms of EDS

Clinical signs of Ehlers-Danlos syndrome

The 11 variants of EDS have genetic, biochemical and clinical differences, but the overlap is extremely common. Clinical features of the condition include:

- Unique appearance of the skin (common to all types)

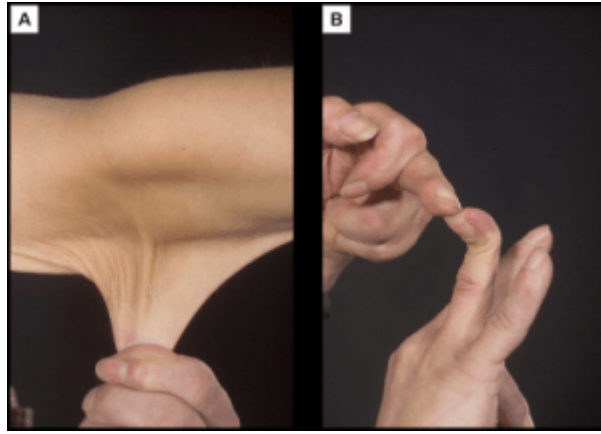


Image: "(A) Prominent hyperextensible skin (B) hypermobile joints." by Openi. License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

- Usually white and soft
- The underlying vessels are often visible
- Hyperextensible
- Molluscoid pseudotumors
 - Small and spongy tumors over pressure points and scars
 - Common in type 1
- Nodules in subcutaneous tissue
 - Small, deep and palpable
 - Opaque bodies on radiographs if calcified
- Poor wound healing
- Fragile dermal skin with bruises and lacerations
- Hyperextensible joints (mostly digits involved)

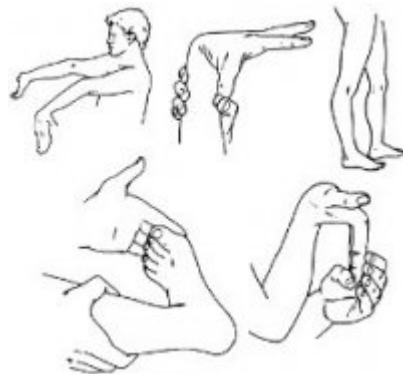


Image: "Ehlers-Danlos syndrome" by [Sammiewood](#) at the English language Wikipedia. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

- Vascular EDS
 - Distinctive facial features
 - Thin nose
 - Thin upper lip
 - Small ear lobes
 - Prominent eyes
 - Thin translucent skin bruising easily
 - Visible vessels especially in fair-skinned people
 - Aorta and arteries to kidneys and spleen weaken, being prone to rupture, which could be fatal.
 - Arteries to the uterus and large intestine also weaken

Diagnosis of EDS

Blood sample to confirm clinical diagnose of EDS

While clinical features are enough to diagnose the condition, genetic testing on a blood sample from the patient can easily confirm the diagnosis. Biochemical studies can help in determining the type. Imaging tests reveal:

- Calcified small, deep, movable and palpable nodules in subcutaneous tissue seen as opacities on radiograph film

Biopsy of skin specimens presents variable, and at times, normal histology. Findings include:

- Disorderly arranged dermal collagen fibers with a whorled appearance
- Irregular size and disoriented elastic fibers
- Electron microscopy reveals
 - Striation defects in collagen fibers with small or large fibrils.

Beighton score	
1 point	If while standing forward bending you can place palms on the ground with legs straight.
1 point	For each elbow that bends backward.
1 point	For each knee that bends backward.
1 point	For each thumb that touches the forearm when bent backward.
1 point	For each little finger that bends backwards beyond 90 degrees.

Differential Diagnosis of EDS

Similar syndromes to Ehlers-Danlos

While suspecting EDS, make sure you rule out the following conditions:

- Turner syndrome
- Cartilage-hair hypoplasia syndrome
- Loeys-Dietz syndrome
- Muscular hypotonia
- Cutis laxa

Therapy of EDS

Palliative management of Ehlers-Danlos syndrome

As already mentioned, there is **no cure** for the condition. Management is **palliative** and involves:

- Wearing a **MedicAlert bracelet** making identification easy in case of arterial rupture.
- Monitoring patients with scoliosis. Instruct them to:
 - Avoid strenuous exercise and lifting
 - Carry out physical therapy
- Cardiac evaluation including ECG, echo and aorta monitoring

- Noninvasive visualization of arterial tree in vascular EDS patients
- High dose vitamin C to improve wound healing
- Recombinant factor VIIa to help control surgical bleeding
- Pre-pregnancy identification of the condition to assess maternal and fetal complications
- Surgery is indicated for the treatment of
 - Dislocations
- Screening for myopia and retinal tears requires an ophthalmologist consultation.
- Comprehensive and accurate genetic counseling

Progress and Prognosis of EDS

While prognosis depends on the type of the syndrome, early diagnosis certainly increases the life span and improves life quality. People with classical and hypermobile types have a normal lifespan, but sudden death is not uncommon in people with vascular EDS.

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