

Ehlers-Danlos Syndrome

Ehlers Danlos Syndrome (EDS) is subdivided into several subtypes (types I-VIII) with different inheritance patterns and collagen gene mutations. The most common and/ or significant EDS types (I-IV and VI) are described below.

Epidemiology

- Prevalence ~1/5000
- EDS type III (hypermobility) is the most common and is usually mild
- EDS type IV is uncommon but is a serious disorder

Genetics

- Classical EDS (types I, II): autosomal dominant, *COL5A1* and *COL5A2* gene mutations, encoding type V collagen
- Hypermobility EDS (type III): autosomal dominant, gene unknown
- Vascular EDS (type IV): autosomal dominant, *COL3A1* gene mutations, encoding type III collagen
- Kyphoscoliosis EDS (type VI): autosomal recessive, *PLOD1* gene mutations causing lysyl hydroxylase deficiency

Clinical presentation

Patients may present with:

- Skin: fragility, easy bruising, thin atrophic scars
- Joints: hypermobility, premature osteoarthritis.
- Intestinal perforation; bladder, uterine and arterial rupture (type IV)

Physical Signs

Classical EDS (types I, II)

- Skin: soft, thin atrophic scars, bruising
- Joints: hyperextensible
- Varicose veins

Hypermobility (type III)

- Skin: soft
- Joints: hyperextensible, recurrent dislocations

Vascular (type IV)

- Subcutaneous fat loss
- Pinched nose
- Thin lips
- Hollowed cheeks
- Skin thin and translucent, veins often visible
- Limited large joint hyperextensibility

Kyphoscoliosis (type VI)

- Skin: soft and hyperextensible
- Joints: hypermobile
- Muscle hypotonia
- Scoliosis

Diagnosis

- Based on medical history, family history and clinical features.
- Consider skin biopsy for EM analysis and fibroblast culture for collagen studies
- Echocardiogram for MVP and aortic root diameter
- Genetic testing: mutation analysis is available for vascular EDS (type IV) and kyphoscoliosis EDS (type VI).

Complications

- Aortic root dilatation (Types I, II 33%; type III 20%)
- Premature osteoarthritis
- Premature labour, post-partum haemorrhage (types I, II)
- Optic globe rupture (type VI)

EDS type IV

- Uterine, bowel and arterial rupture
- Complications occur in at least 25% of individuals after 20 years of age and 80% before 40 years of age.
- Arterial repair not always technically possible.
- Shortened life expectancy, median 48 years.

Treatment

- There is no specific treatment to alter the progression of EDS.
- Modified management in pregnancy and during labour
- Offer clinical genetics/counselling advice

Surveillance

- Echocardiogram to monitor aortic root dilatation
- MRI scan of aorta to detect aneurysmal dilatation in EDS IV

Differential Diagnosis

- Benign joint hypermobility syndrome
- Cutis Laxa: loose skin, abnormality of elastic fibres
- Marfan syndrome: hypermobile joints, lens dislocation, aortic root dilatation
- Rare EDS subtypes, e.g. arthrochalasia (type VIIA and B) with congenital hip dislocation; dermatosporaxis (type VIIC) with severe skin fragility; X-linked EDS (type V)

BOX1 : Beighton Score

The 9-point Beighton score is used to assess joint hypermobility. One point is scored for each side of the body for:

- Passive extension of the 5th finger >90 degrees
- Passive apposition of thumb to flexor aspect of the forearm
- Hyperextension of the elbow beyond 10 degrees
- Hyperextension of the knee beyond 10 degrees
- Forward flexion of the trunk with legs straight so that palms rest flat on the floor (one point only).

Pictures
Hyperextension
Abnormal scar
Lax skin
Collagen EM
Face/habitus