Ehlers-Danlos Syndrome Fact Sheet

This document has been created by Genetic Health Queensland as a guide for **clinical assessment of patients with suspected Ehlers-Danlos syndrome (EDS)**.

Hypermobile Ehlers-Danlos syndrome

Joint hypermobility is common in the general population and often familial. The diagnosis of hypermobile Ehlers-Danlos syndrome (hEDS) remains a clinical diagnosis and does not need to be made by a Clinical Geneticist. As there is no known genetic basis for hEDS and genetic contributions are poorly understood, we do not offer genetic testing to patients with confirmed or suspected hEDS.

To make a clinical diagnosis of hEDS, refer to the 2017 International Diagnostic Criteria at The Ehlers-Danlos Society website (www.ehlers-danlos.com/wp-content/uploads/hEDS-Dx-Criteria-checklist-1.pdf).

Management for hEDS is generally designed to alleviate symptoms and should be through referral to relevant medical specialists and allied health professionals. This can include low impact exercise, physiotherapy, psychological support for chronic fatigue and pain management, pain medication tailored to symptoms, and appropriate therapy for any associated stomach or bowel problems. Guidelines for managing patients with hEDS, as well as the clinical features and natural history, can be found at The Ehlers-Danlos Society website (www.ehlers-danlos.com/management-and-care-guidelines).

Other types of Ehlers-Danlos syndrome and connective tissue disorders

There are at least 12 other types of EDS, some of which are associated with life-threatening complications (such as arterial or organ rupture). Additional information regarding the clinical features of EDS types, can be found at The Ehlers-Danlos Society website (www.ehlers-danlos.com/eds-types/).

Clinical genetics assessment and testing is available when other types of EDS are suspected, as well as other connective tissue disorders associated with arterial dissection/aneurysm (such as Marfan Syndrome or Loeys-Dietz syndrome). Refer to Appendix for clinical criteria for other types of EDS and other connective tissue disorders.

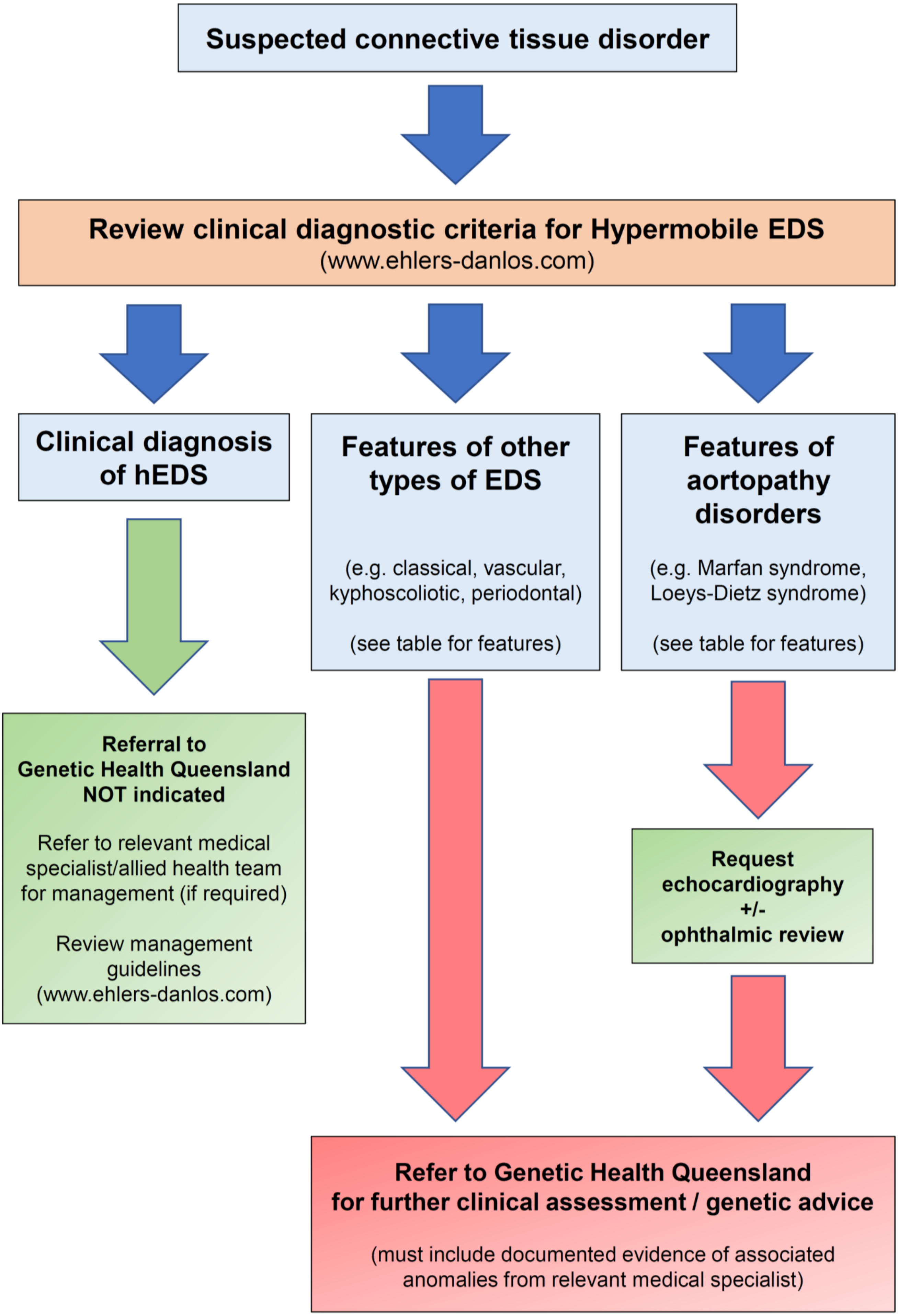
The following clinical features are 'red flags' that would prompt a referral to Clinical Genetics:

- Young onset or unexplained arterial dissection/aneurysms/tortuosity
- Aortic root dilatation (in absence of bicuspid aortic valve)
- Severe progressive cardiac-valvular disease
- Early-onset varicose veins (<30 years)
- Organ rupture
- Extensive atrophic scarring
- Early-onset kyphoscoliosis
- Congenital hand and foot deformities
- Recurrent hernias
- Recurrent spontaneous pneumothoraces
- Severe early-onset periodontitis (childhood or adolescence).

(Must provide documented evidence of features as assessed by a medical specialist).

If you wish to discuss a potential referral, please contact Genetic Health Queensland on (07) 3646 1686.

Assessment and referrals



Appendix: Clinical criteria for selected connective tissue disorders

Condition	Major criteria	Minor criteria
Classical EDS (cEDS)	Skin hyperextensibility and atrophic scarring Generalised joint hypermobility	• Easy bruising • Soft, doughy skin • Skin fragility (or traumatic splitting) • Molluscoid pseudotumors • Subcutaneous spheroids • Hernia • Epicanthal folds • Complications of joint hypermobility (sprains, dislocations/subluxations, pain, flexible flat foot) • Family history of a first-degree relative who meets clinical criteria
Classical-like EDS (clEDS)	Skin hyperextensibility (with velvety skin texture and absence of atrophic scarring) Generalised joint hypermobility (with/without recurrent dislocations) Easy bruising/spontaneous ecchymoses	• Foot deformities (broad/plump forefoot, brachydactyly with excessive skin, pes planus, hallux valgus, piezogenic papules) • Oedema in legs (in the absence of heart failure) • Mild proximal and distal muscle weakness • Axonal polyneuropathy • Muscle atrophy (hands and feet) • Acrogeria, mallet fingers, clinodactyly, brachydactyly • Vaginal/uterus/rectal prolapse
Vascular EDS (vEDS)	Arterial rupture (at young age) Spontaneous sigmoid colon rupture (in absence of other bowel pathology) Uterine rupture during the 3rd trimester (in absence of previous C-section and/or severe peripartum perineum tears) Carotid-cavernous sinus fistula formation (in absence of trauma) Family history of vEDS (with documented causative variant in *COL3A1*)	• Easy bruising (with minimal trauma and/or unusual sites) • Thin, translucent skin with increased venous visibility • Characteristic facial appearance • Spontaneous pneumothorax • Acrogeria • Talipes equinovarus • Congenital hip dislocation • Hypermobility of small joints • Tendon and muscle rupture • Keratoconus • Gingival recession and fragility • Early-onset varicose veins (<30 years and nulliparous if female)
Cardio-valvular EDS (cvEDS)	Severe progressive cardiac-valvular problems (aortic valve, mitral valve) Skin involvement (skin hyperextensibility, atrophic scars, thin skin, easy bruising) Joint hypermobility (generalized or restricted to small joints)	• Inguinal hernia • Pectus deformity (especially excavatum) • Joint dislocations • Foot deformities (pes planus, pes planovalgus, hallux valgus)

Condition	**Major criteria**	**Minor criteria**
Arthrochalasia EDS (aEDS)	Congenital bilateral hip dislocation Severe generalised joint hypermobility (with multiple subluxations/dislocations) Skin hyperextensibility	• Muscle hypotonia • Kyphoscoliosis • Radiologically mild osteopenia • Tissue fragility (including atrophic scarring) • Easy bruising
Dermatosparaxis EDS (dEDS)	Extreme skin fragility (congenital or postnatal skin tears) Characteristic craniofacial features Redundant (almost lax) skin (with excessive skin folds at wrist/ankles) Increased palmar wrinkling Severe bruising (with risk of subcutaneous haematomas and haemorrhage) Umbilical hernia Postnatal growth retardation Short limbs, hands, and feet Perinatal complications (due to excessive skin fragility)	• Soft, doughy skin • Skin hyperextensibility • Atrophic scarring • Generalised joint hypermobility • Complications of visceral fragility (bladder rupture, diaphragmatic rupture, rectal prolapse) • Delayed motor development • Osteopenia • Hirsutism • Tooth abnormalities • Refractive errors (myopia, astigmatism) • Strabismus
Kyphoscoliotic EDS (kEDS)	Congenital muscular hypotonia Congenital or early-onset kyphoscoliosis (progressive or nonprogressive) Generalised joint hypermobility with dislocations/subluxations	• Skin hyperextensibility • Easy bruising • Rupture/aneurysm of a medium-sized artery • Osteopenia/osteoporosis • Blue sclerae • Hernia (umbilical or inguinal) • Pectus deformity • Marfanoid habitus • Talipes equinovarus • Refractive errors (myopia, hypermetropia) • Skin fragility (easy bruising, friable skin, poor wound healing, widened atrophic scarring) • Scleral and ocular fragility/rupture • Microcornea • Facial dysmorphology • Muscle atrophy • Follicular hyperkeratosis • Bladder diverticula • Congenital hearing impairment (sensorineural, conductive, or mixed)

Condition	Major criteria	Minor criteria
Spondylodysplastic EDS (spEDS)	Short stature (progressive in childhood) Muscle hypotonia (severe congenital to mild later-onset) Bowing of limbs	• Skin involvement (skin hyperextensibility, soft/doughy skin, thin skin) • Pes planus • Delayed motor development • Osteopenia • Delayed cognitive development
Musculocontractural EDS (mcEDS)	Congenital multiple contractures (characteristically adduction-flexion contractures and/or talipes equinovarus) Characteristic facial features (evident at birth or in early infancy) Characteristic cutaneous features (skin hyperextensibility, easy bruising, skin fragility with atrophic scars, increased palmar wrinkling)	• Recurrent/chronic dislocations • Pectus deformities (flat, excavatum) • Spinal deformities (scoliosis, kyphoscoliosis) • Peculiar fingers (tapering, slender, cylindrical) • Progressive talipes deformities (valgus, planus, cavum) • Large subcutaneous hematomas • Chronic constipation • Colonic diverticula • Pneumothorax/pneumohemothorax • Nephrolithiasis/cystolithiasis • Hydronephrosis • Cryptorchidism in males • Strabismus • Refractive errors (myopia, astigmatism) • Glaucoma/elevated intraocular pressure
Myopathic EDS (mEDS)	Congenital muscle hypotonia, and/or muscle atrophy (improves with age) Proximal joint contractures (knee, hip and elbow) Hypermobility of distal joints	• Soft, doughy skin • Atrophic scarring • Motor developmental delay • Myopathy on muscle biopsy
Periodontal EDS (pEDS)	Severe and intractable periodontitis of early onset (childhood or adolescence) Lack of attached gingiva Pretibial plaques Family history of a first-degree relative who meets clinical criteria	• Skin hyperextensibility and fragility (wide/atrophic scarring) • Easy bruising • Joint hypermobility (mostly distal joints) • Prominent vasculature • Hernias • Increased rate of infections • Marfanoid facial features • Acrogeria

Condition	Clinical features

Marfan syndrome	• Aortic root enlargement (Z score>2)
	• Ectopia lentis
	• Systemic score ≥ 7
	  ○ Wrist and/or thumb sign
	  ○ Pectus carinatum/excavatum or chest asymmetry
	  ○ Hindfoot deformity
	  ○ Pes planus
	  ○ Pneumothorax
	  ○ Dural ectasia
	  ○ Protrusio acetabulae
	  ○ Reduced upper segment to lower segment AND increased arm span to height ratios
	  ○ Scoliosis or thoracolumbar kyphosis
	  ○ Reduced elbow extension
	  ○ Characteristic facial appearance (dolichocephaly, downslanting palpebral fissures, enophthalmos, malar hypoplasia, and retrognathia)
	  ○ Skin striae
	  ○ Myopia
	  ○ Mitral valve prolapse

Loeys-Dietz syndrome (LDS)	• Vascular
	  ○ Dilatation or dissection of aorta and other arteries
	  ○ Other arterial aneurysms and tortuosity
	• Skeletal
	  ○ Pectus excavatum/carinatum, scoliosis, joint laxity or contracture (typically fingers), arachnodactyly, talipes equinovarus, cervical spine malformation and/or instability, osteoarthritis
	• Craniofacial
	  ○ Widely spaced eyes, bifid uvula / cleft palate, craniosynostosis (any sutures)
	• Cutaneous
	  ○ Soft and velvety skin, translucent skin with increased venous visibility, easy bruising, dystrophic scars, milia (prominently on face)
	• Allergic/inflammatory disease
	  ○ Food allergies, seasonal allergies, asthma/chronic sinusitis, eczema, eosinophilic esophagitis/gastritis, inflammatory bowel disease
	• Blue or dusky sclerae