GP Fact Sheet: Genetic Testing

Joint Hypermobility / Ehlers Danlos Syndrome

Joint hypermobility is common. It affects 1-4% of people and is often familial. Joint hypermobility varies in severity from simple joint hypermobility to Hypermobility Ehlers Danlos Syndrome (hEDS). Most people with joint hypermobility can be managed through their GP and do not need a genetics assessment.

Please see the attached information and referral guidelines for patients with joint hypermobility. A small proportion of people with joint hypermobility do need to be seen by a clinical geneticist for assessment and consideration of genetic testing. This group usually has additional distinctive clinical features or "red flags." Usually an echocardiogram (to rule out dilatation of the ascending aorta or mitral valve prolapse) and an eye examination by an ophthalmologist or experienced optometrist (to rule out lens dislocation or high grade myopia) will be needed to complete the assessment.

Patients with hypermobility who do not meet these referral criteria can be assessed clinically for hypermobility-type Ehlers Danlos syndrome (hEDS) using the guidelines provided in the attached information sheet.

Genetic testing for hypermobility-type EDS is not helpful as causative single gene mutations have not been identified in the vast majority of people with this condition. People with hypermobility benefit from physical, psychological and pain-based therapies and utilisation of local allied health, pain and psychological services for management may be considered.

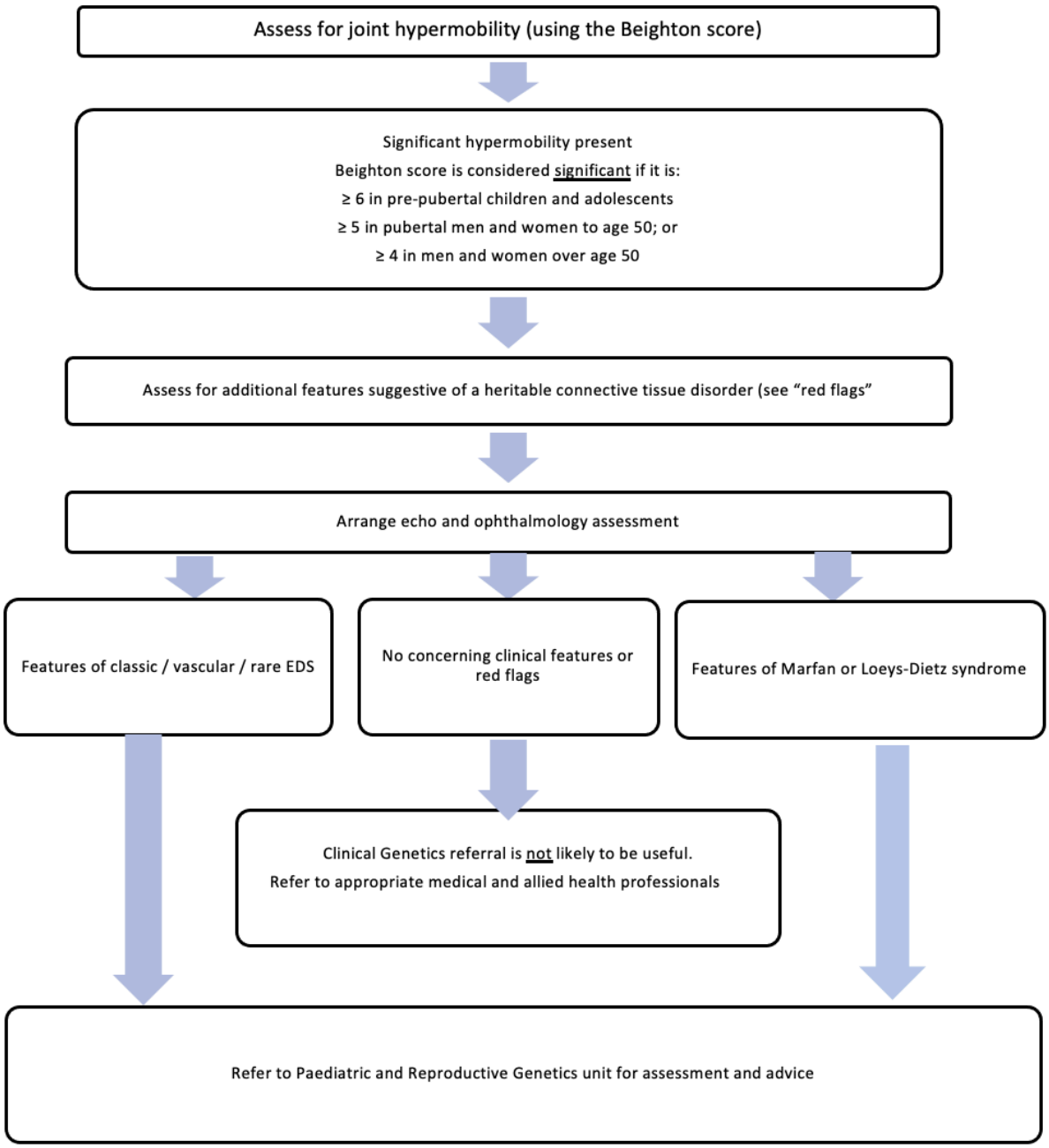
Referral to a genetics service is appropriate for any person fulfilling the referral criteria as such individuals may have a different connective tissue disorder, other than hEDS. Where applicable, we would welcome a referral with details of your assessment and any relevant investigation or specialist medical reports for these individuals.

If you have any questions, you can contact the Paediatric and Reproductive Genetics Unit on 8161 7375.

GP Fact Sheet: Genetic Testing

Joint Hypermobility / Ehlers Danlos Syndrome

Guidelines for Referring People with Joint Hypermobility to Genetics Services



For more information
Paediatric Reproductive Genetics Unit
Women's and Children's Hospital
72 King William Rd, North Adelaide SA 5006
Telephone (08) 8161 7000

Reviewed: March 2023

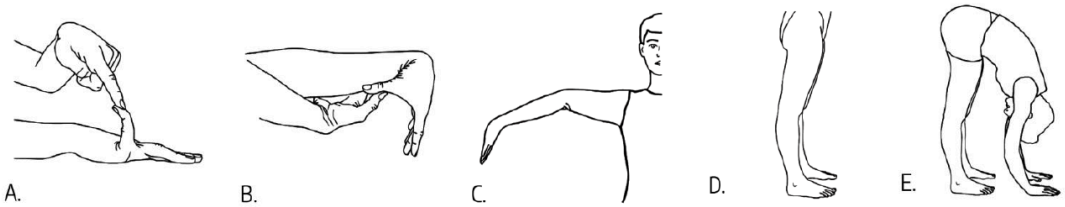
Government of South Australia
Women's and Children's Health Network

GP Fact Sheet: Genetic Testing

Joint Hypermobility / Ehlers Danlos Syndrome

1. Assess for Joint Hypermobility using the Beighton Score:

	Feature	points	score
A	LITTLE FINGERS: dorsiflexion beyond 90 degrees Rest palm and forearm on a flat surface with palm down and fingers out straight. Can the 5th finger be bent upwards at the knuckle to go back beyond 90 degrees?	1 point each finger	
D	THUMBS: apposition to flexor aspect of the forearm Stand with arm out straight, palm facing down, and the wrist fully bent downward Can the thumb be pushed back to touch the forearm?	1 point each thumb	
B	ELBOWS: hyperextension beyond 10 degrees Stand with arms outstretched and palms facing upwards. Does the elbow extend more than an extra 10 degrees beyond neutral?	1 point each elbow	
A	KNEES: hyperextension beyond 10 degrees Stand with knees locked (bent backwards as far as possible). Does the lower part of either leg extend more than 10 degrees forward from neutral?	1 point each knee	
C	SPINE: hyper-flexibility Stand with knees locked, bend forward. Can place palms of both hands flat on the floor in front of feet without bending knees?	1 point	
	Beighton score		



The Beighton score is considered significant if it is:

≥6 in pre-pubertal children and adolescents; or

≥5 in pubertal men and women to age 50; or

≥4 men and women over the age of 50.

For more information
Paediatric Reproductive Genetics Unit
Women's and Children's Hospital
72 King William Rd, North Adelaide SA 5006
Telephone (08) 8161 7000

Reviewed: March 2023

GP Fact Sheet: Genetic Testing

Joint Hypermobility / Ehlers Danlos Syndrome

2. For individuals with significant joint hypermobility as assessed in Step 1: Assess for additional features suggestive of a heritable connective tissue disorder and "red flags" – see below

System	"Red Flag" clinical features
Skin	Widened, atrophic scars Marked skin hyperextensibility Skin fragility Thin, translucent skin Redundant, sagging skin Easy bruising (spontaneous or with minimal trauma)
Body habitus	Marfanoid body habitus Distinctive facial features (thin lips, prominent eyes, narrow nose)
Skeletal	Progressive and severe scoliosis / kyphosis Congenital bilateral hip dislocation
Vascular	Aortic (or other arterial) aneurysm / rupture / dissection Young onset thoracic aortic dilation Unexplained extensive varicosities at young age (varicose veins) Bicuspid aortic valve Mitral valve prolapse with regurgitation
Ocular	Lens dislocation High grade myopia
Oral	Severe periodontal disease Lack of attached gingiva
Other	Spontaneous pneumothorax Cleft palate / bifid uvuvla Bowel perforation Uterine or other organ rupture Muscle or tendon rupture
Family history	Family history of "red flags" Family history of sudden, unexplained death

For more information
Paediatric Reproductive Genetics Unit
Women's and Children's Hospital
72 King William Rd, North Adelaide SA 5006
Telephone (08) 8161 7000

Reviewed: March 2023

Government of South Australia
Women's and Children's
Health Network

GP Fact Sheet: Genetic Testing

Joint Hypermobility / Ehlers Danlos Syndrome

3. Assess for the presence of other features that suggest hEDS (see diagnostic check sheet below)

4. Referral to a Genetics service is appropriate for any person with **significant joint hypermobility (as outlined in Step 1 <u>and</u> any personal or family history of features outlined in Step 2**

For more information
Paediatric Reproductive Genetics Unit
Women's and Children's Hospital
72 King William Rd, North Adelaide SA 5006
Telephone (08) 8161 7000

Reviewed: March 2023

GP Fact Sheet: Genetic Testing

Joint Hypermobility / Ehlers Danlos Syndrome

The International Consortium on Ehlers-Danlos Syndromes & Related Disorders
In Association with The Ehlers-Danlos Society

Diagnostic Criteria for Hypermobile Ehlers-Danlos Syndrome (hEDS)

This diagnostic checklist is for doctors across all disciplines to be able to diagnose EDS

Distributed by The Ehlers Danlos Society.

Patient name: _____ DOB: _____ DOV: _____ Evaluator: _____

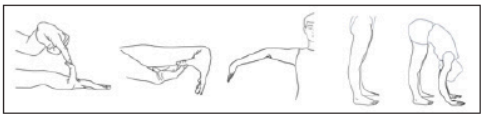
The clinical diagnosis of hypermobile EDS needs the simultaneous presence of all criteria, 1 ***and*** 2 ***and*** 3.

CRITERION 1 – Generalized Joint Hypermobility

One of the following selected:

- ☐ ≥6 pre-pubertal children and adolescents
- ☐ ≥5 pubertal men and woman to age 50
- ☐ ≥4 men and women over the age of 50

Beighton Score: ____/9



If Beighton Score is one point below age- and sex-specific cut off, two or more of the following must also be selected to meet criterion:

- ☐ Can you now (or could you ever) place your hands flat on the floor without bending your knees?
- ☐ Can you now (or could you ever) bend your thumb to touch your forearm?
- ☐ As a child, did you amuse your friends by contorting your body into strange shapes or could you do the splits?
- ☐ As a child or teenager, did your shoulder or kneecap dislocate on more than one occasion?
- ☐ Do you consider yourself "double jointed"?

CRITERION 2 – Two or more of the following features (A, B, or C) must be present

Feature A (five must be present)

- ☐ Unusually soft or velvety skin
- ☐ Mild skin hyperextensibility
- ☐ Unexplained striae distensae or rubae at the back, groins, thighs, breasts and/or abdomen in adolescents, men or pre-pubertal women without a history of significant gain or loss of body fat or weight
- ☐ Bilateral piezogenic papules of the heel
- ☐ Recurrent or multiple abdominal hernia(s)
- ☐ Atrophic scarring involving at least two sites and without the formation of truly papyraceous and/or hemosideric scars as seen in classical EDS
- ☐ Pelvic floor, rectal, and/or uterine prolapse in children, men or nulliparous women without a history of morbid obesity or other known predisposing medical condition
- ☐ Dental crowding and high or narrow palate
- ☐ Arachnodactyly, as defined in one or more of the following:
  (i) positive wrist sign (Walker sign) on both sides, (ii) positive thumb sign (Steinberg sign) on both sides
- ☐ Arm span-to-height ratio ≥1.05
- ☐ Mitral valve prolapse (MVP) mild or greater based on strict echocardiographic criteria
- ☐ Aortic root dilatation with Z-score >+2

Feature A total: ____/12

Feature B

- ☐ Positive family history; one or more first-degree relatives independently meeting the current criteria for hEDS

Feature C (must have at least one)

- ☐ Musculoskeletal pain in two or more limbs, recurring daily for at least 3 months
- ☐ Chronic, widespread pain for ≥3 months
- ☐ Recurrent joint dislocations or frank joint instability, in the absence of trauma

CRITERION 3 – All of the following prerequisites MUST be met

1. Absence of unusual skin fragility, which should prompt consideration of other types of EDS
2. Exclusion of other heritable and acquired connective tissue disorders, including autoimmune rheumatologic conditions. In patients with an acquired CTD (*e.g.* Lupus, Rheumatoid Arthritis, etc.), additional diagnosis of hEDS requires meeting both Features A and B of Criterion 2. Feature C of Criterion 2 (chronic pain and/or instability) cannot be counted toward a diagnosis of hEDS in this situation.
3. Exclusion of alternative diagnoses that may also include joint hypermobility by means of hypotonia and/or connective tissue laxity. Alternative diagnoses and diagnostic categories include, but are not limited to, neuromuscular disorders (*e.g.* Bethlem myopathy), other hereditary disorders of the connective tissue (e.g. other types of EDS, Loeys-Dietz syndrome, Marfan syndrome), and skeletal dysplasias (*e.g.* osteogenesis imperfecta). Exclusion of these considerations may be based upon history, physical examination, and/or molecular genetic testing, as indicated.

Diagnosis: _____

v9

Paediatric Reproductive Genetics Unit
Women's and Children's Hospital
72 King William Rd, North Adelaide SA 5006
Telephone (08) 8161 7000

Reviewed: March 2023

Government of South Australia
Women's and Children's Health Network

GP Fact Sheet: Genetic Testing

Joint Hypermobility / Ehlers Danlos Syndrome

Resources for people with joint hypermobility

Online resources

- The Sydney Children's Hospital Network fact sheet on hypermobility.
  - https://www.schn.health.nsw.gov.au/fact-sheets/joint-hypermobility
- Information about joint hypermobility from the UK National Health Service.
  - NHS - Joint Hypermobility Syndrome
  - NHS Inform - Joint Hypermobility
- Information about joint hypermobility from the American College of Rheumatology.
  - Hypermobility Syndrome
- Hypermobility Connect
  - https://www.hypermobilityconnect.com/
- Hypermobility Syndromes Association
  - https://www.hypermobility.org/

Online articles

- Guidelines for Management of Joint Hypermobility Syndrome in Children and Young People. Compiled by the Allied Health Professionals Group of the British Society for Paediatric and Adolescent Rheumatology (BSPAR, 2012).
  - Management of Syndromic Hypermobility: A Systematic Literature Review
- Hypermobile Ehlers–Danlos Syndrome (a.k.a. Ehlers–Danlos Syndrome Type III and Ehlers–Danlos Syndrome Hypermobility Type): Clinical Description and Natural History (Am J Med Genet Part C 2017;175C:48–69)
  - Hypermobile Ehlers-Danlos Syndrome Clinical Description and History
- The Evidence-Based Rationale for Physical Therapy Treatment of Children, Adolescents, and Adults Diagnosed With Joint Hypermobility Syndrome/Hypermobile Ehlers Danlos Syndrome (Am J Med Genet Part C 2017;175C:158-167)
  - Physical Therapy Treatment of Children, Adolescents, and Adults with Joint Hypermobility Syndrome/Hypermobile Ehlers Danlos Syndrome

For more information
Paediatric Reproductive Genetics Unit
Women's and Children's Hospital
72 King William Rd, North Adelaide SA 5006
Telephone (08) 8161 7000

Reviewed: March 2023

Government of South Australia
Women's and Children's Health Network