JOINT HYPERMOBILITY AND THE EHLERS-DANLOS SYNDROMES

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Disclosures

- I am the owner of Healed and Empowered LLC, a health education and consulting company for people with chronic pain and comorbid conditions
- Some medications and therapies discussed are off-label
- No other disclosures to report

Learning Objectives

- At the conclusion of this session, participants should be able to:
  - Recognize the clinical features and complications of Hypermobile type Ehlers-Danlos Syndrome(hEDS)
  - Understand diagnostic criteria associated with the Ehlers-Danlos Syndromes
  - Describe interprofessional treatment and management of patients with Hypermobile type Ehlers-Danlos Syndrome (hEDS)

EDS in the Media

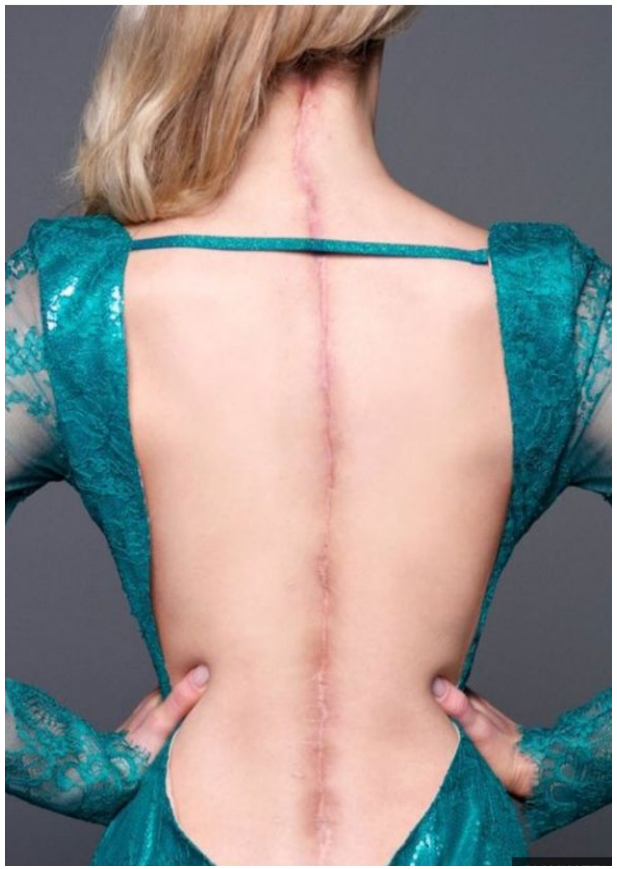
http://www.eightlimbyoga.com/contortionist-pictures/

https://themighty.com/2016/12/self-acceptance-model-ehlers-danlos-syndrome/

http://www.gumbyworld.com

http://www.goodhousekeeping.com/life/entertainment/g2720/guinness-world-records-60th-anniversary/

EDS in Real Life



> NO OTHER DISEASE IN THE HISTORY OF MODERN MEDICINE, HAS BEEN NEGLECTED IN SUCH A WAY AS EHLERS-DANLOS SYNDROME
>
> PROFESSOR RODNEY GRAHAME

The Ehlers-Danlos Society

What are the Ehlers-Danlos Syndromes?

- Family of autosomal dominant inherited connective tissue disorders (CTD)
- Inappropropriate collagen deposition/remodeling
- "generally characterized by joint **hypermobility**, skin **hyperextensibility**, and tissue **fragility**." –Ehlers-Danlos Society

- Now considered a group of syndrome<u>S</u> consisting of 14 different subtypes

The Ehlers-Danlos syndromes

NAME OF EDS SUBTYPE	INHERITANCE	GENETIC BASIS
Classical EDS (cEDS)	AR	*COL5A1, COL5A2* (rarely *COL1A1*)
Classical-like EDS (clEDS)	AR	*TNXB*
Cardiac-valvular EDS (cvEDS)	AR	*COL1A2*
Vascular EDS (vEDS)	AD	*COL3A1* (rarely *COL1A1*)
Hypermobile EDS (hEDS)	AD	Unknown
Arthrochalasia EDS (aEDS)	AD	*COL1A1, COL1A2*
Dermatosparaxis EDS (dEDS)	AR	*ADAMTS2*
Kyphoscolitic EDS (kEDS)	AR	*PLOD1* *FKBP14*

AD = autosomal dominant; AR = autosomal recessive

www.ehlers-danlos.com/eds-types/

The Ehlers-Danlos syndromes

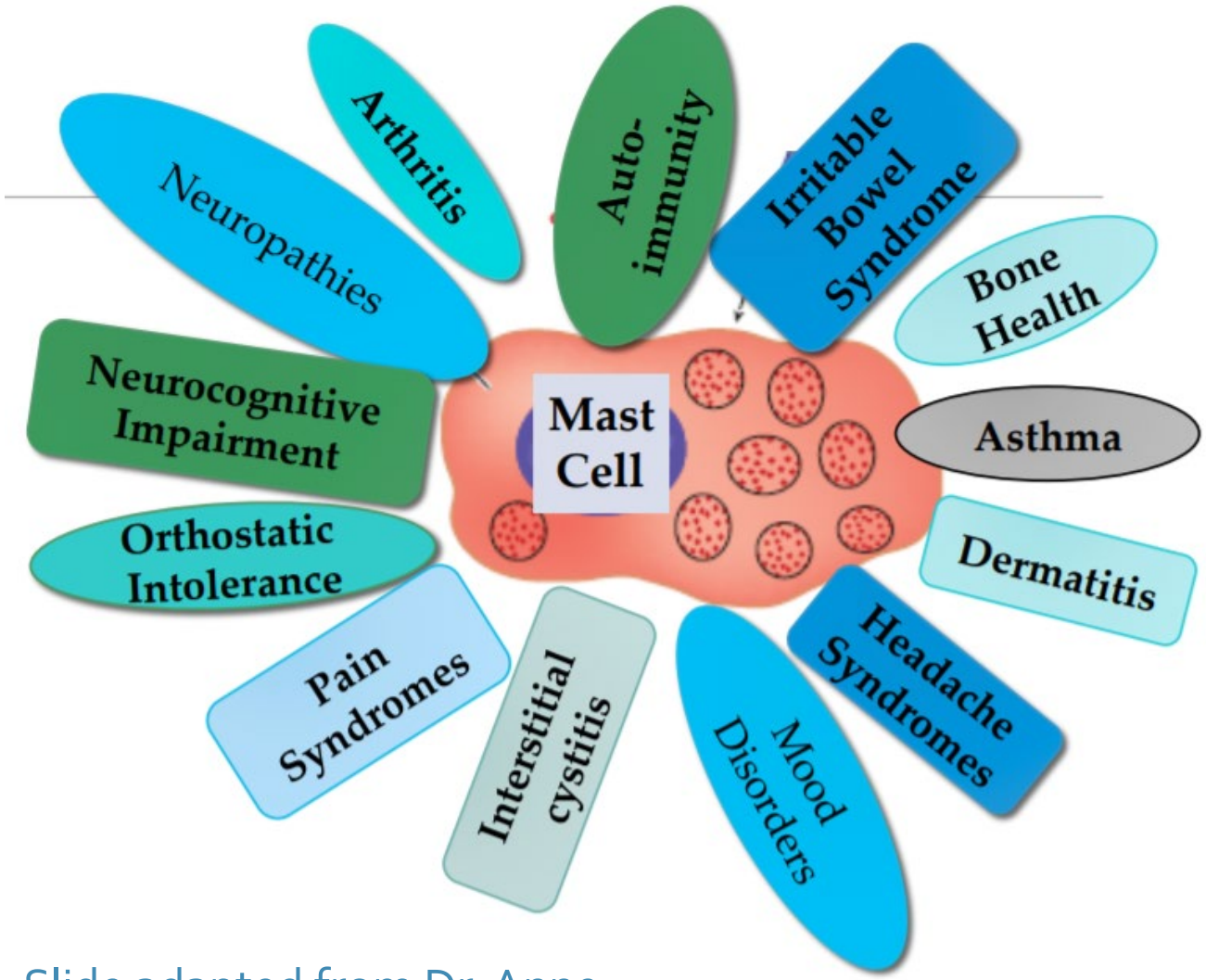
NAME OF EDS SUBTYPE	INHERITANCE	GENETIC BASIS
Brittle cornea syndrome (BCS)	AR	*ZNF469* *PRDM6*
Spondylodysplastic EDS (spEDS)	AR	*B4GALT7* *B3GALT6* *SLC39A13*
Musculocontractual EDS (mcEDS)	AR	*CHST14* *DSE*
Myopathic EDS (mEDS)	AD or AR	*COL12A1*
Periodontal EDS (pEDS)	AD	*C1R*

AD = autosomal dominant; AR = autosomal recessive

www.ehlers-danlos.com/eds-types/

Hypermobile EDS (hEDS)

- ***80-90% of EDS***
- hEDS has more strict dx criteria as of March 2017
- hEDS is considered the extreme end of the hypermobile spectrum disorders (HSD)
- **hEDS is the only type of EDS with no genetic marker (yet!)**
- Inappropriate mast cell activation is linked with hEDS



Adapted from Theoharides, NEJM 2015

Slide adapted from Dr. Anne Maitland, EDS Global Learning Conference 2019

- Mast Cells Release:
  - Histamine
  - Interleukins
  - Prostaglandins
  - Pro-inflammatory cytokines
- Patients with hEDS have a high rate of comorbidities such as GI d/o, asthma, neuropsyciatric conditions, OI, chronic pain
- Increased Mast Cell content in the undamaged skin of patients with signs of CTD

What is the average time that a patient with hEDS waits before receiving a correct diagnosis?

A. 1 year

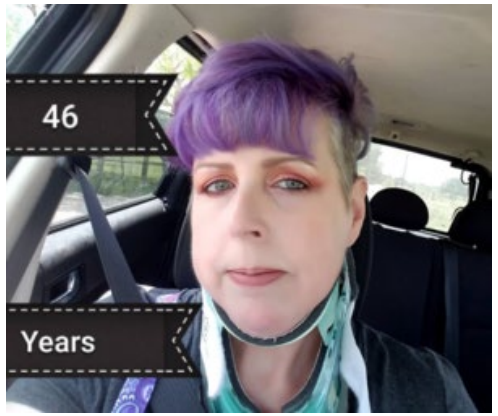
B. 7 years

C. 10 years

D. 14 years

Answer:

D. 14 years

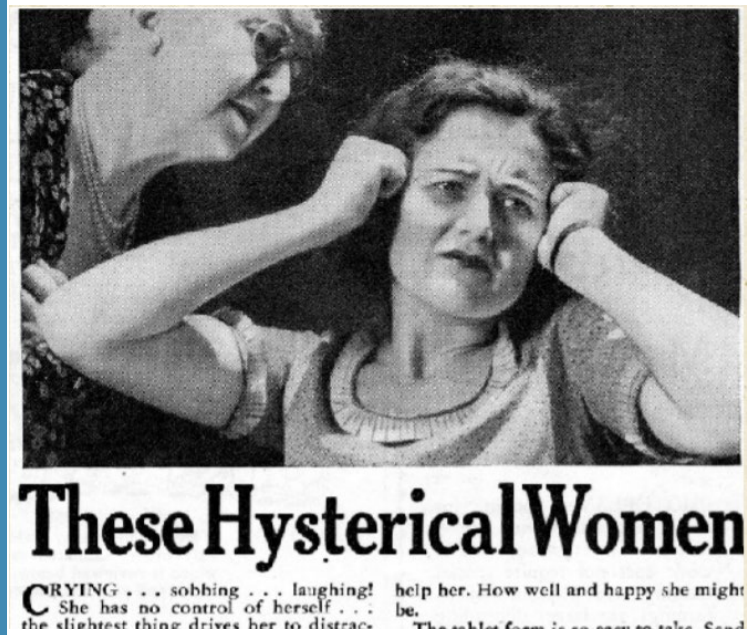


https://www.mindbodyeds.org.uk/whatwedo

https://www.mindbodyeds.org.uk/myedsdiagnosis-2

Epidemiology

- hEDS: 1 in 2500 - 1 in 5000, females> males
  HSD: 7.5/1,000 to 20/1,000 (0.75–2%)
- Underdiagnosed and often misdiagnosed
  - 80% w/o diagnosis = 4/5 people
  - 12-20 year time to diagnosis



These Hysterical Women

CRYING . . . sobbing . . . laughing! She has no control of herself . . . help her. How well and happy she might be.

Epidemiology

Total responses : **2544**

Number of Countries: **26**

2016 EDS Survey Question #18:

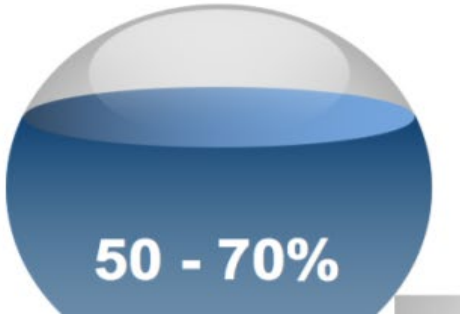
Q18: What statements reflect your EXPERIENCE being diagnosed with EDS?

97% reported that previous doctors…

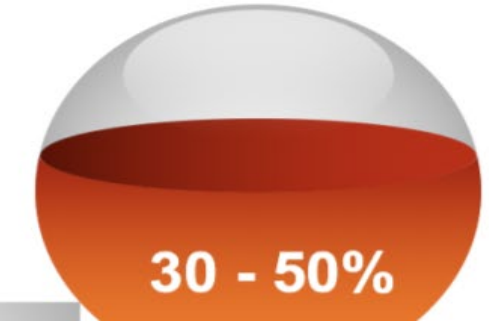
"labeled them with a psychological condition to explain EDS symptoms"

Anxiety Disorders and the Joint Hypermobility S.

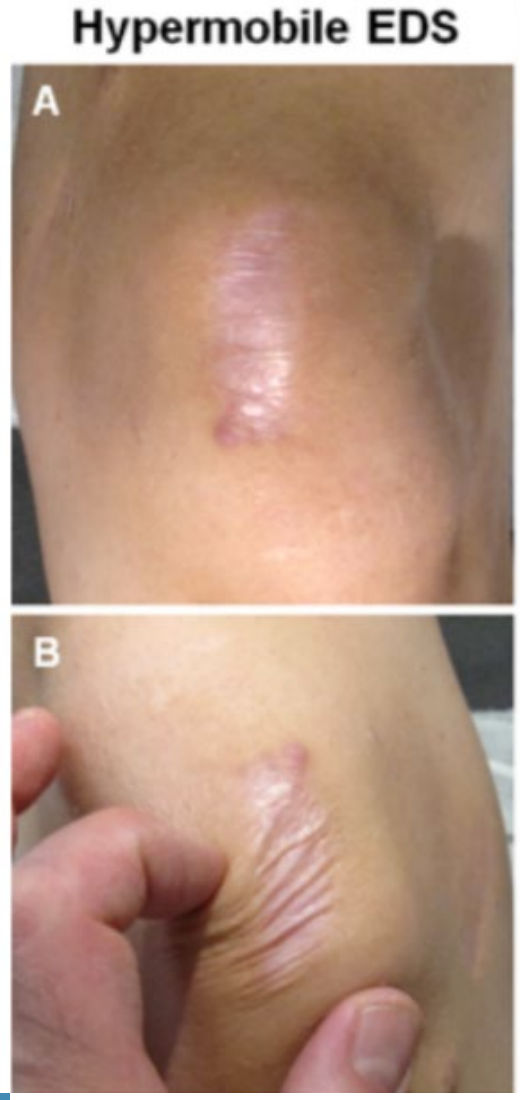
Joint Hypermobility Syndrome in Anxiety Disorders



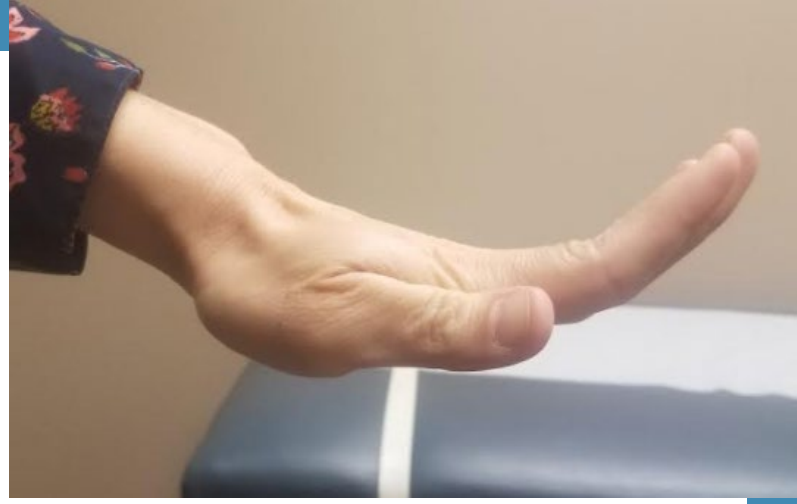
Anxiety Disorder in the Joint Hypermobility Syndrome

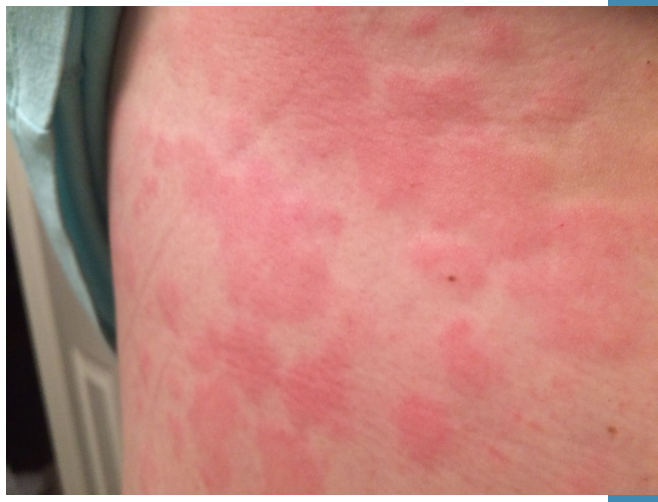


Clinical Manifestations



- Hypermobility
  - Laxity & instability + pain, ± fatigue.
  - Can affect all joints, including costovertebral and craniocervical
- Pain
  - Increasing pain, increasing fatigue
  - "fibromyalgia" and psych diagnoses
  - Stiffness ↑ with age (↓ hypermobility)
- Other systemic involvement
  - Skin, Cardiac, Neurological
  - Part of diagnostic criteria





Multisystem Involvement

- **Musculoskeletal**
  - OA and DDD/ spondylopathy
  - Craniocervical instability
- **Skin changes**
  - Atrophic scars
  - Piezogenic Papules of the heel
  - Recurrent hernias
- **Neurological**
  - Sleep disturbance
  - Anxiety/ depression
  - Chiari/ tethered cord/ CSF leak
  - Small fiber neuropathy
  - Clumsiness/ falls
  - Proprioceptive difficulty

Multisystem Involvement

Cardiovascular

- Venous pooling/ Aneurysm formation
- Aortic dilatation/ Mitral valve prolapse
- POTS

Endocrine

- Increased Epinephrine
- Dysautonomia

ENT

- Vision changes
- Dysphagia
- Gum disease/ TMJ

GI/ GU

- Hiatal hernia, GI dysmotility, N/V/C/D
- Pelvic organ prolapse

True or False?

- Patients always need genetic testing to confirm a diagnosis of hypermobile Ehlers-Danlos Syndrome (hEDS).

False

- hEDS can be diagnosed without genetic testing if there is low suspicion for other types of EDS or CTD

Diagnosis

The Ehlers-Danlos Society™

THE BEIGHTON SCORE

How to Assess Joint Hypermobility

A numerical mobility score of 0 to 9, one point allocated for the ability to perform each of the following tests:

Pull little finger back beyond 90°
(one point for each side)

Bend knee backwards beyond 10°
(one point for each side)

Pull thumb back to touch forearm
(one point for each side)

Lie hands flat on floor while keeping knees straight and bending forward at waist

Bend elbow backwards beyond 10°
(one point for each side)

A positive Beighton score for adults is 5 out of the 9 possible points; for children, a positive score is at least 6 out of 9 points.

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

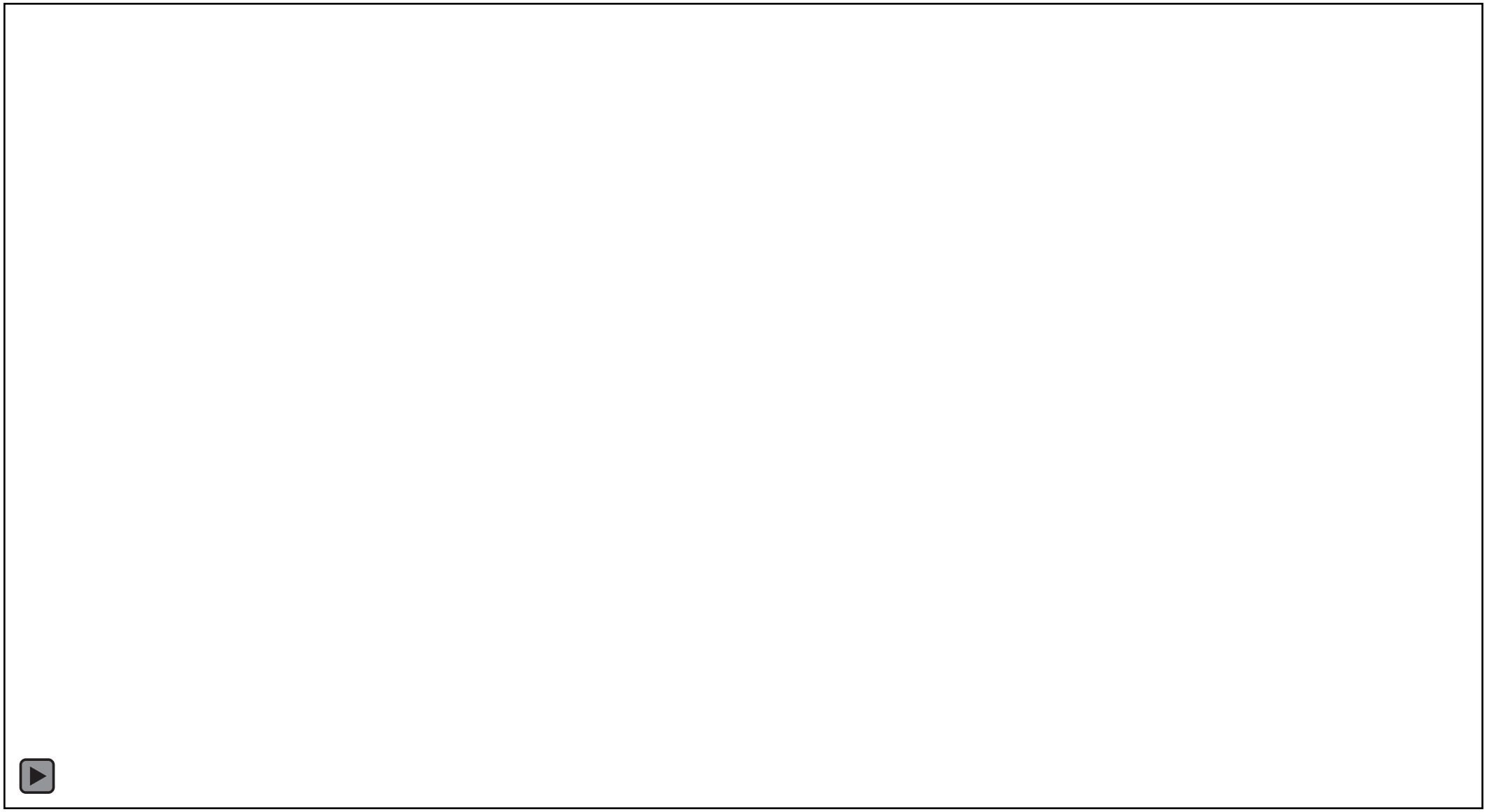
Feature B
- ☐ Positive family history; one or more first-degree relatives independently meeting the current criteria for hEDS

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.

https://www.youtube.com/watch?v=rmrjZKskW7o



Diagnosis – in 3 steps

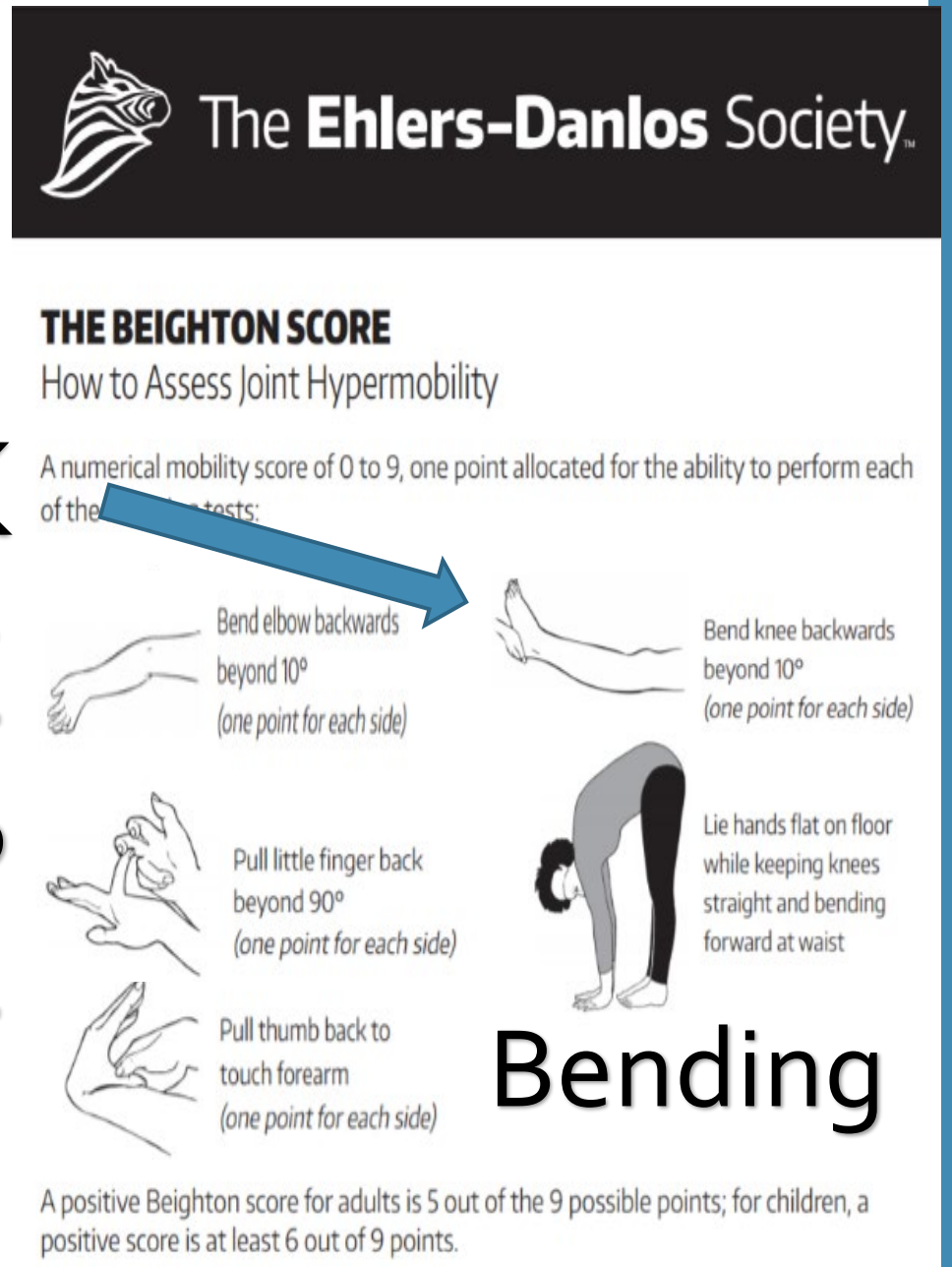
Step 1: Beighton Score ≥5/9

- 5 pt questionnaire
- ≥5/9 = HSD

Step 2: Features A, B, C

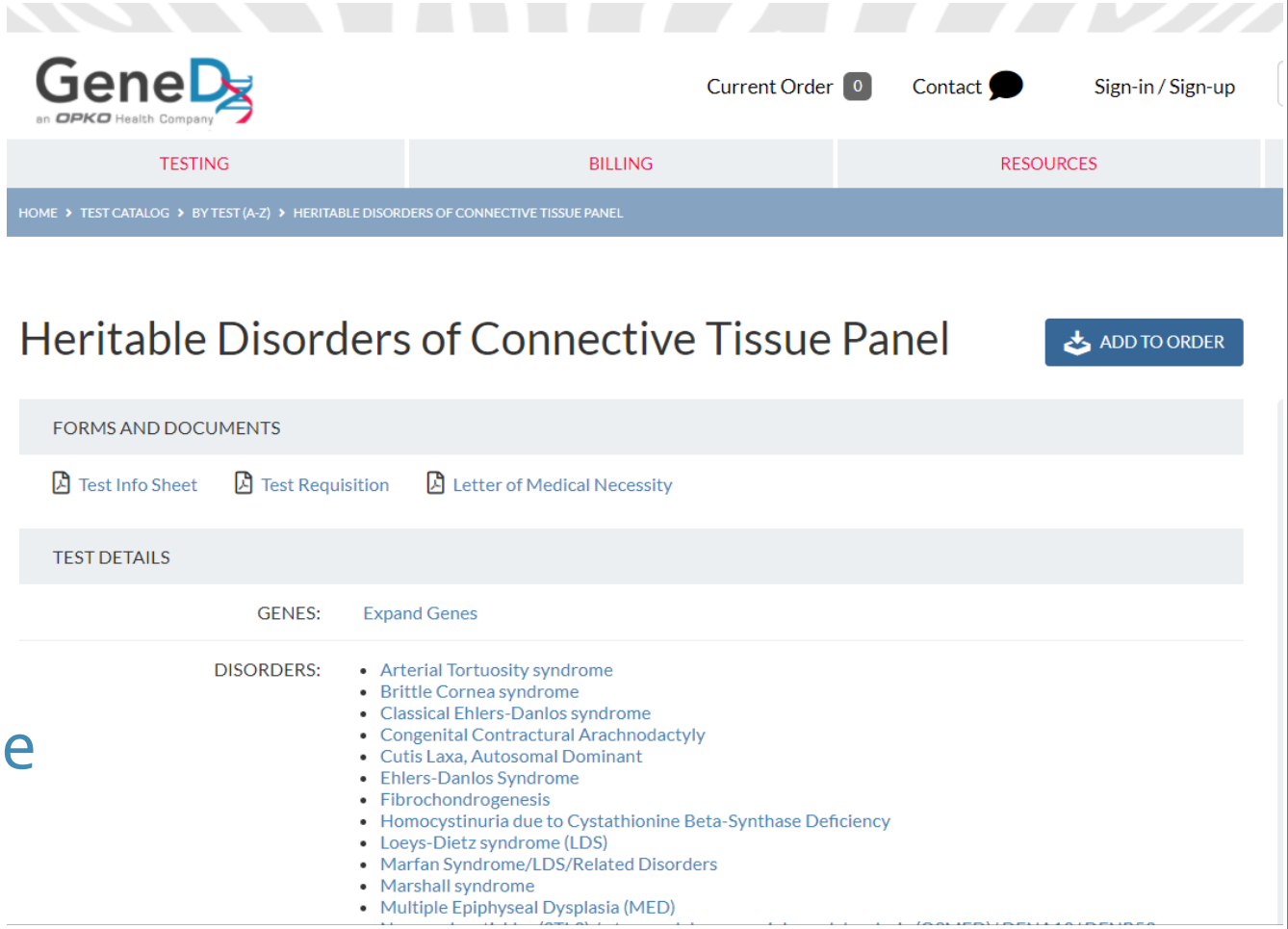
- A: Systemic manifestations
- B: Family History
- C: MSK complications

Step 3: Exclude other Dx



Differential Diagnoses

- Other types of EDS
- Osteogenesis imperfecta
- Marfan Syndrome
- Loeys-Dietz syndrome
- Arterial tortuosity syndrome
- Lateral meningocele syndrome



Now What?

https://pixabay.com/en/teamwork-team-gear-board-chalk-2499638/

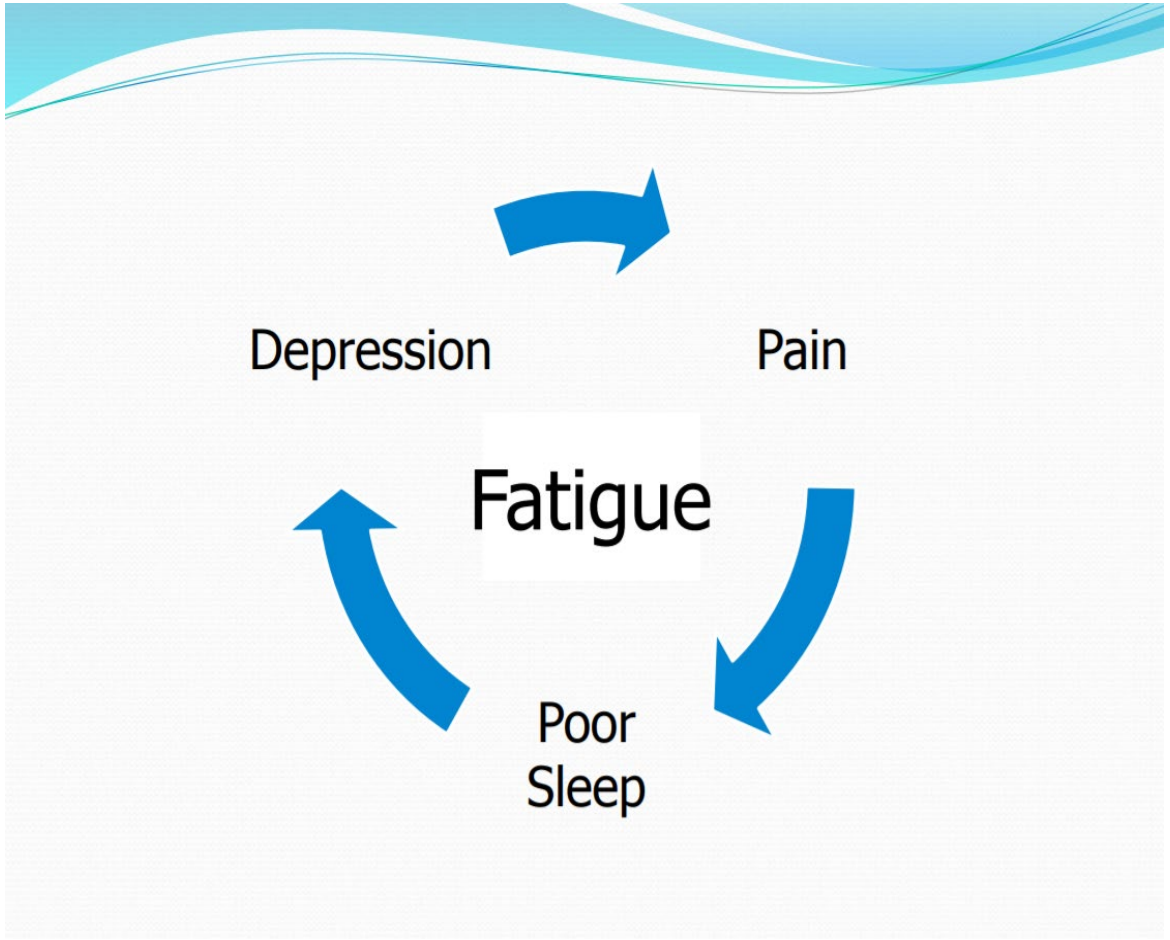
Multidisciplinary Team

- Pain Management
- Physical therapy
- Neurosurgery
- Orthopedics
- Genetics
- Cardiology
- Orthopedist
- Immunology
- Pulmonology
- Rheumatology
- Neurology
- Urology
- Dermatology
- Ophthalmology
- Otolaryngology
- Psychology/ Psychiatry
- Sleep center
- Caregiver/ home support

http://www.aib.edu.au/blog/teamwork/teamwork-is-important-in-the-workplace/

Outpatient Management in hEDS

- Individual treatment plan
- Big 3:
  - Pain
  - Depression
  - Sleep disturbance
- Address all 3 together



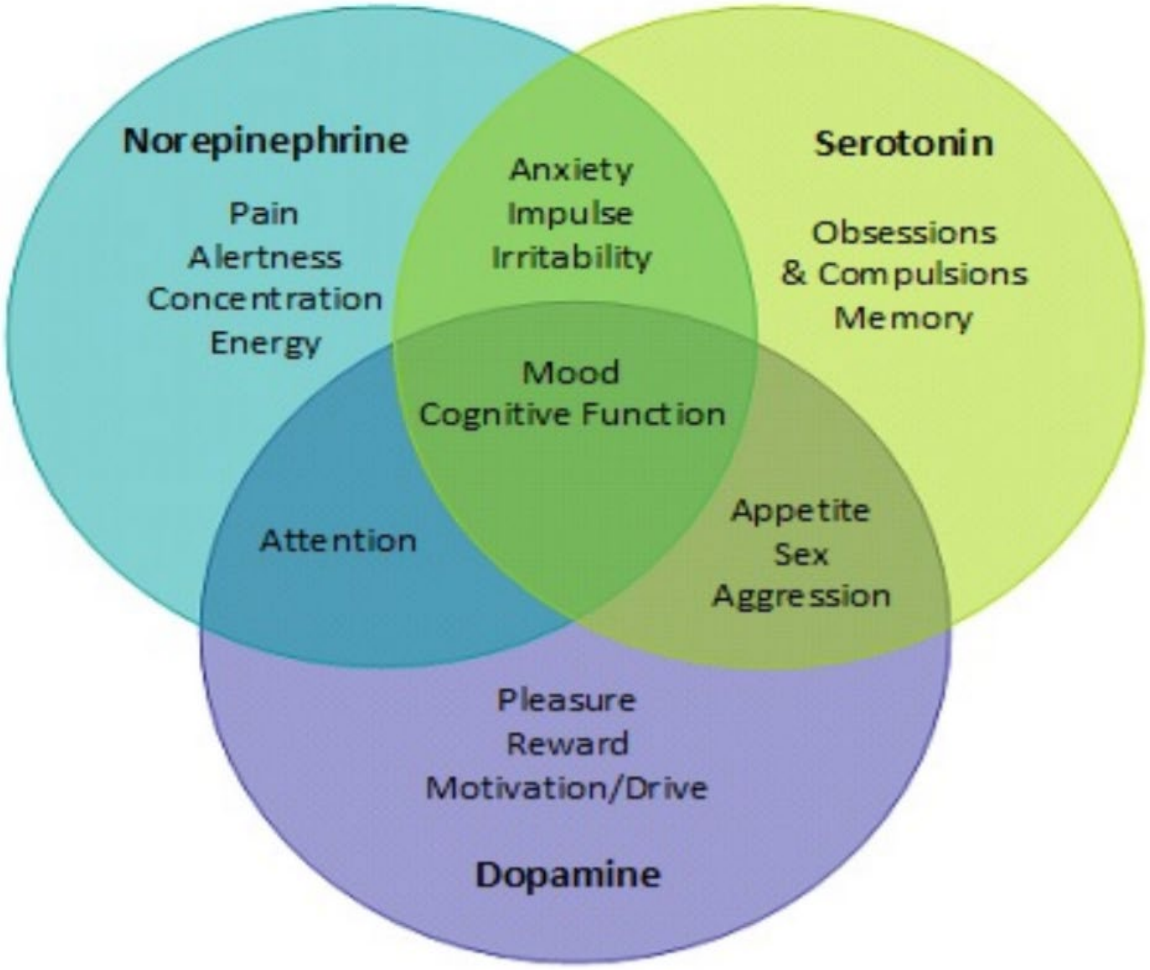
https://www.ehlers-danlos.com/wp-content/uploads/Pocinki-Evaluation-and-Management-of-Fatigue-in-Patients-with-Ehlers-Danlos-Syndrome-S.pdf

Sleep Management

- Sleep Hygiene
  - Pregnancy pillow
  - Adjustable beds
  - Meditation
  - Stabilize joints
- Medication
  - Block extra epinephrine (beta and alpha blockers, clonidine)
  - Offset extra epinephrine (benzodiazepines, SSRI's)
  - Increase deep sleep (trazodone, amitryptiline, mirtazepine)

Depression Management

- Behavioral
  - CBT/ biofeedback
  - Mindfulness
  - Support Groups
  - Counseling
  - Service Animals
- Pharmacological
  - Serotonergic- SSRI
  - Noradrenergic- SNRI
  - Dopaminergic (bupropion)
  - Ketamine
  - Cannabis



Source: Deplin™ pamphlet

Pain Management

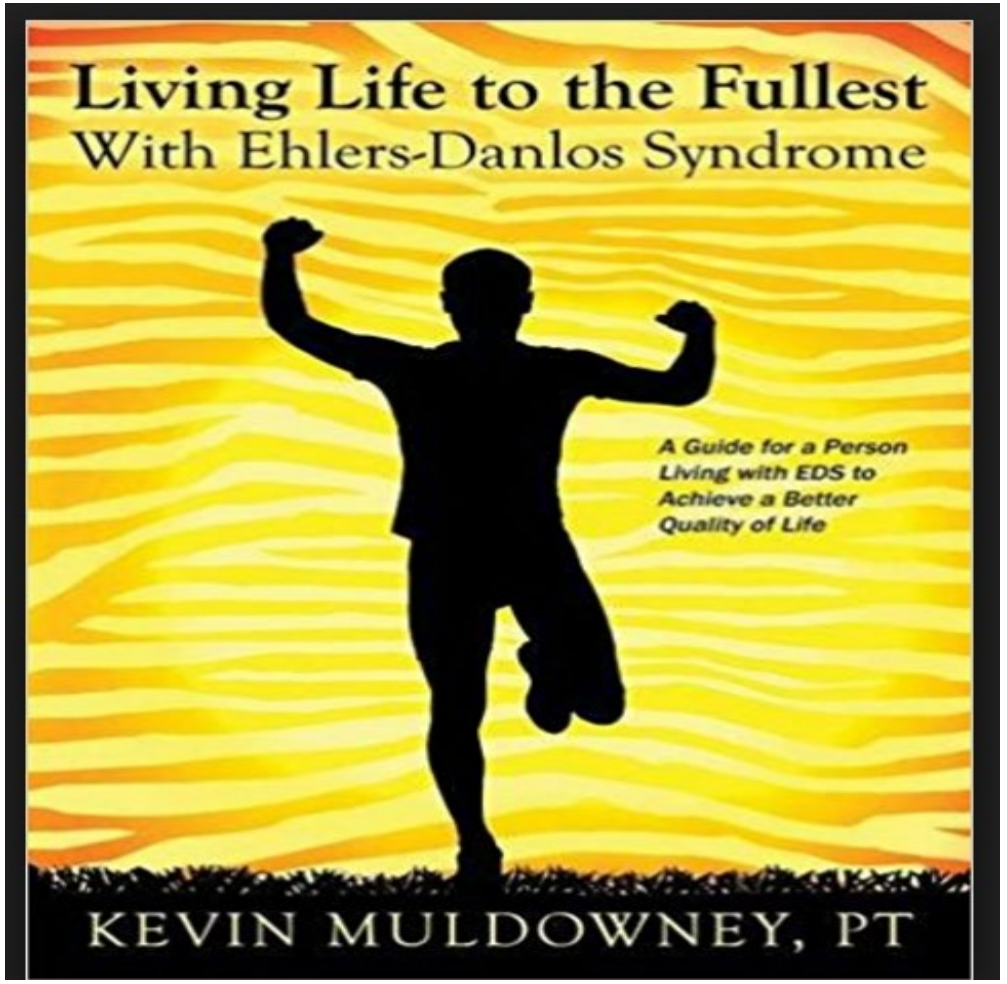
- Radiographs often not helpful
- Treat Source of pain
  - Mechanical:
    - muscle relaxers, physical measures, injection therapy, bracing
  - Inflammatory: NSAIDs, Steroids prn
    - Examine nutrition/ supplements
    - Cannabis may be helpful
  - Mast cell: Antihistamines
  - Neurological: SNRI/ AED

NOTE:

- Opioids if necessary
  - May worsen GI symptoms
  - Rapid metabolizers = may need higher medication doses

Pain Management

- Prevent deconditioning
  - Bracing- not contraindicated in EDS patients
  - Physical Therapy
    - Refer to a PT with experience with hypermobile patients
  - Home Exercise
  - Consistency is key!



Additional Management Considerations

Management Considerations

- Rapid metabolizer
  - Consider genetic testing for meds
- Chiari/ CSF leak/ Craniocervical Instability
  - Need UPRIGHT MRI with flexion/ extension
  - MR Myelogram or CT myelogram
- Early spondylopathy, OA, DDD, scoliosis
- SI joint dysfunction
  - does not correlate with imaging
- Aortic root dilation

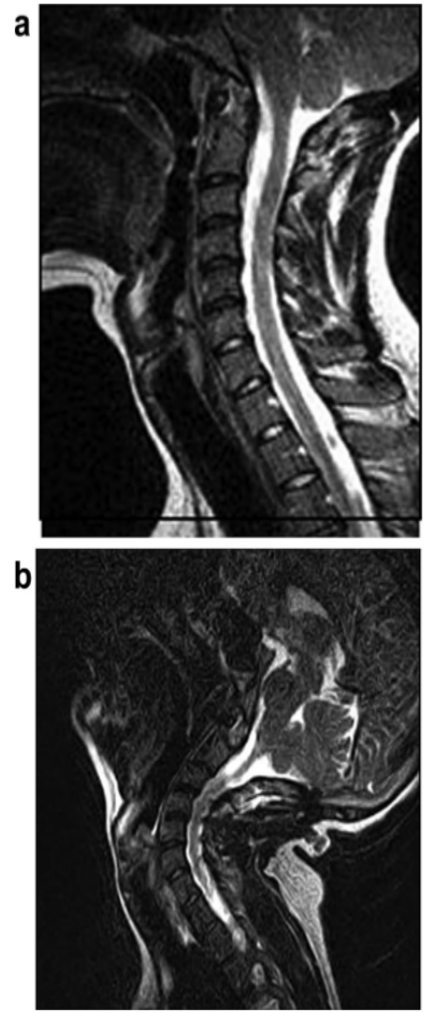


Figure 4. **a**: Segmental cervical instability, showing widespread degenerative disc disease characteristic of EDS-HT, but no spinal cord compression on neutral view (Sagittal view, T2 weighted MRI of the cervical spine in the neutral position). **b**: Dynamic instability evident upon extension of the neck, showing postero-listhesis of C4 on C5, causing spinal cord compression (MRI sagittal view of the cervical spine, T2 weighted).

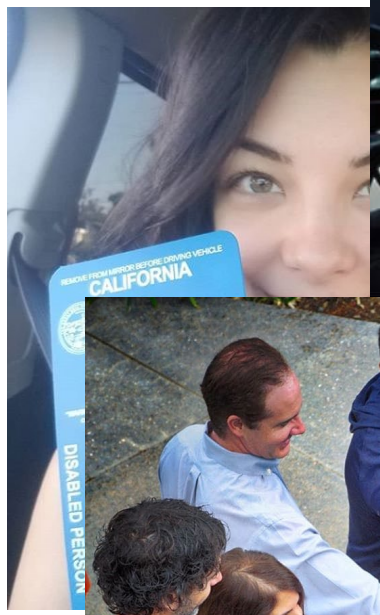
Surgical Considerations

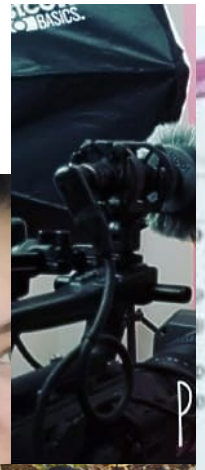
- Pre-op
  - Screen for Aortic root dilation
- Anesthesia
  - Rapid metabolizer of local anesthesia and pain meds
- Head positioning/ Intubation
  - CCI
  - Pharyngeal laxity
  - TMJ
- Bandaging or tourniquet
  - Skin tears, compartment syndrome
- Recovery
  - Venous pooling--> DVT
  - Caution during transfers
  - Scarring

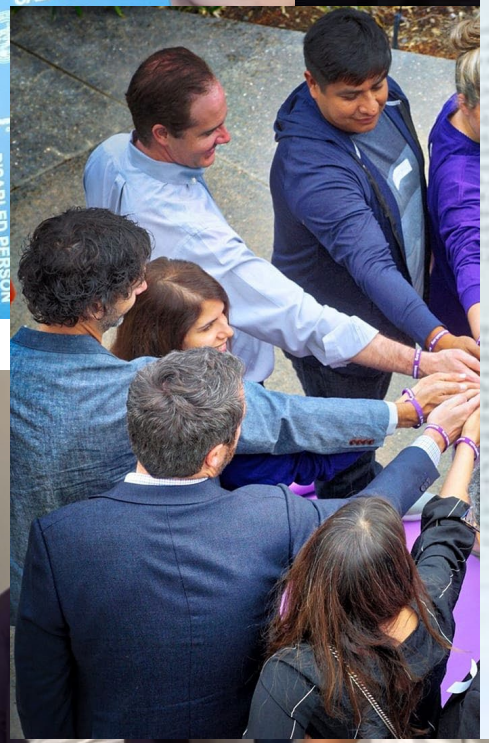
Wiesmann et al:
Recommendations for anaesthesia and perioperative management in patients with Ehlers-Danlos Syndrome(s)

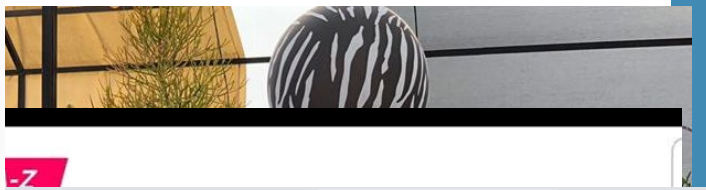
Take Home Points

- Recognize the clinical features and complications of Hypermobile type Ehlers-Danlos Syndrome(hEDS)
- Understand diagnostic criteria associated with the Ehlers-Danlos Syndromes
- Describe interprofessional treatment and management of patients with Hypermobile type Ehlers-Danlos Syndrome (hEDS)
- Healthcare providers can screen for EDS in 30 seconds
- There is a growing network of specialists to whom you can refer patients with EDS









Physician Assistants: The All-Star
Healthcare | Upland, CA | Healed
Dashboard | Wix.com
La Verne Email
Bates
Bates' Guide to Phy...
Brianna Cardenas N...

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paint your pain.html
video EDS 1.mp4
video EDS 2.mp4

Chronic pain affects 1 in 3 Americans[6], and is

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QUESTIONS?

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