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Bendy Bodies, Ehlers Danlos Syndromes Unmasked

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Disclosures:

- Speakers' Bureau: AbbVie & Averitas

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Objectives:

- Define the diagnosis of Ehlers-Danlos syndrome(s).
- State main differences in the current 2017 diagnostic criteria.
- Identify three effective treatment strategies for pain associated with Hypermobility Ehlers-Danlos syndrome (hEDS), including use of pharmacotherapies.

Types of Ehlers-Danlos Syndrome

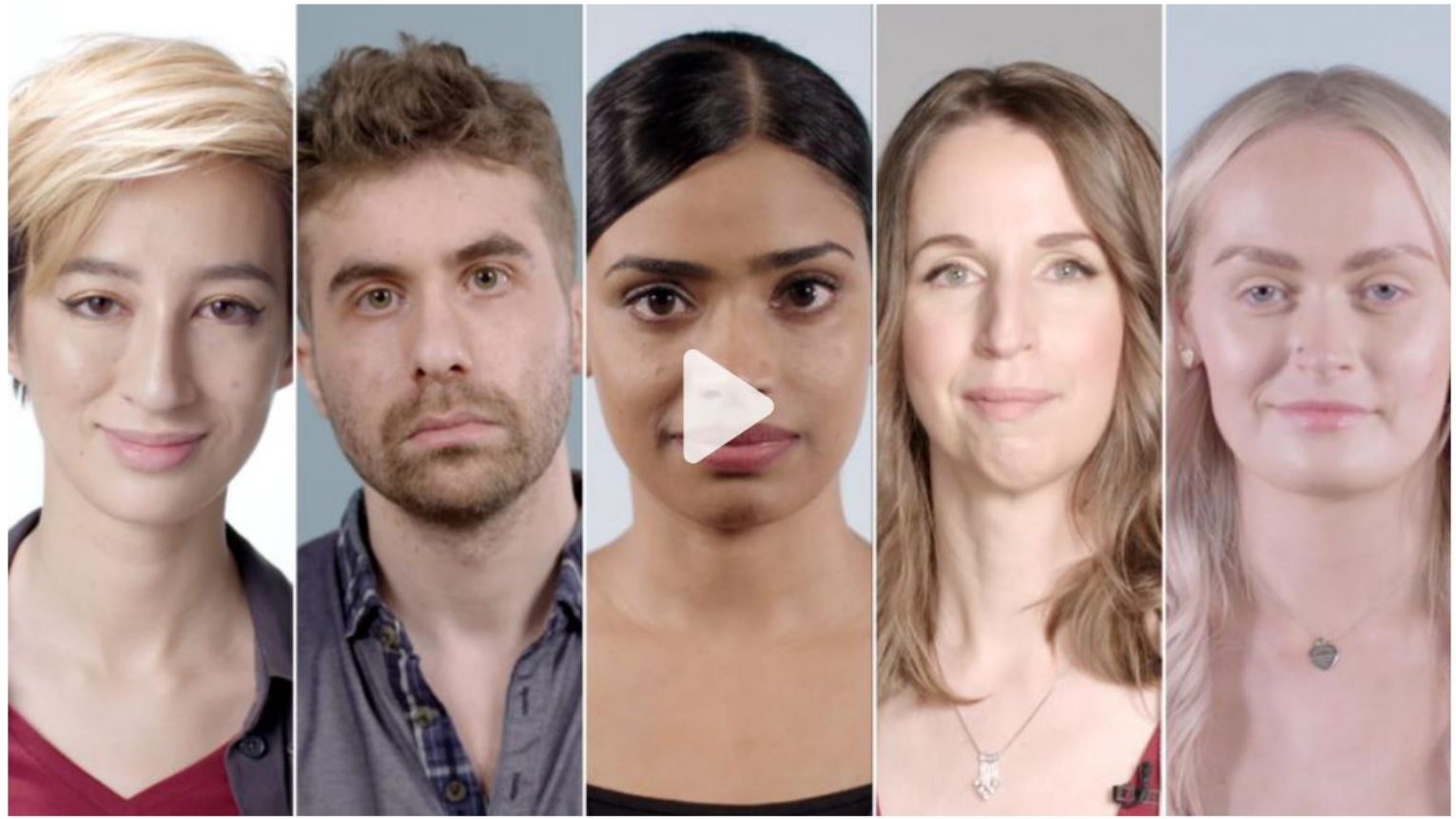
Early 1900's: Edward Ehlers & Henri Danlos described "cutis laxa"

1945 Ehlers Danlos Syndrome was cointed

1960's Berlin nosology identified 11 numbered subtypes of EDS

1998 Villefranche nosology changed EDS to 6 subtypes w/descriptive names

2017 EDS International Consortium listed 13 subtypes of EDS



https://www.cnn.com/videos/health/2022/12/16/ehlers-danlos-syndrome-patient-stories-contd-lon-orig.cnn

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Healthcare experiences among adults w/ hEDS & hypermobility spectrum disorder

Cross-sectional mixed-method study → Hypothesized that many individuals would report low satisfaction with healthcare and low health-related quality of life → that lower healthcare satisfaction would be related to lower health-related quality of life & self-efficacy for symptom management.

(N= 2125) completed an online survey:

(Estrella & Frazier, 2024)

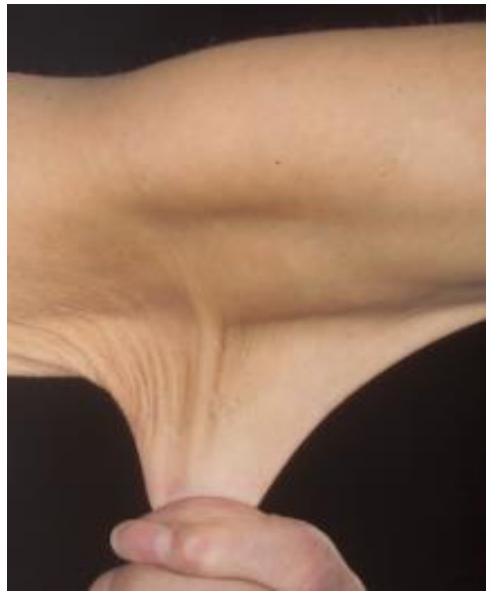
- Satisfaction with healthcare
- Health-related quality of life
- Symptom management self-efficacy
- Qualitative data also were gathered on desired changes to improve healthcare

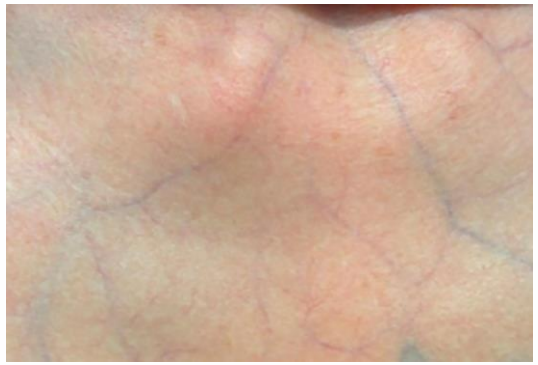
Results:

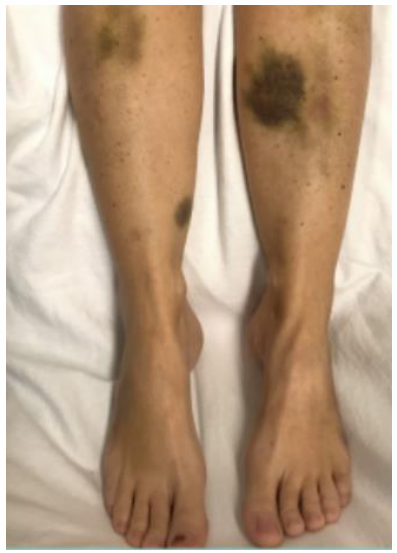
- Participants reported low satisfaction w/ healthcare & lower health-related qol & symptom management self-efficacy than norm groups.
- Lower satisfaction w/ healthcare was associated w/ lower health-related quality of life and lower symptom management self-efficacy.
- The most common desired change to improve healthcare was more knowledge about hEDS and HSD among healthcare professionals.

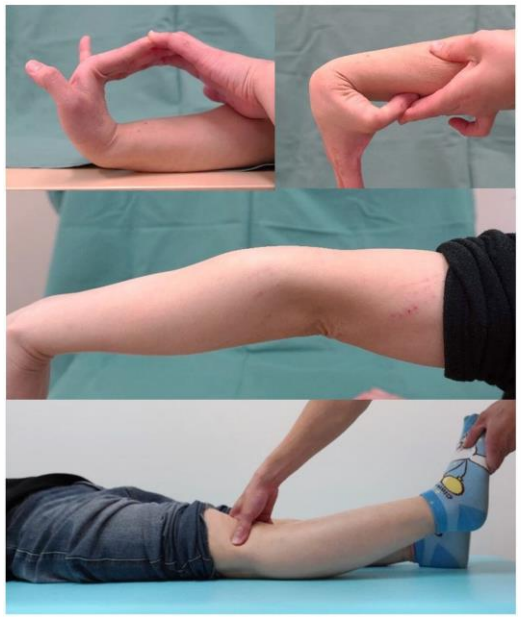
Ehlers-Danlos syndromes (EDSs) are a heterogeneous group of inheritable connective tissue disorders characterized by :

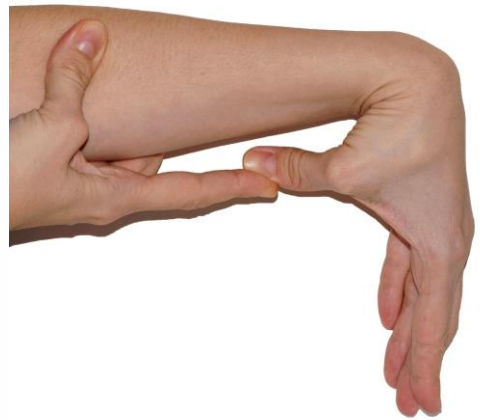
- Skin hyper elasticity
- Hypermobility of joints
- Atrophic scarring & cutaneous/dermal manifestations
- Fragility of blood vessels









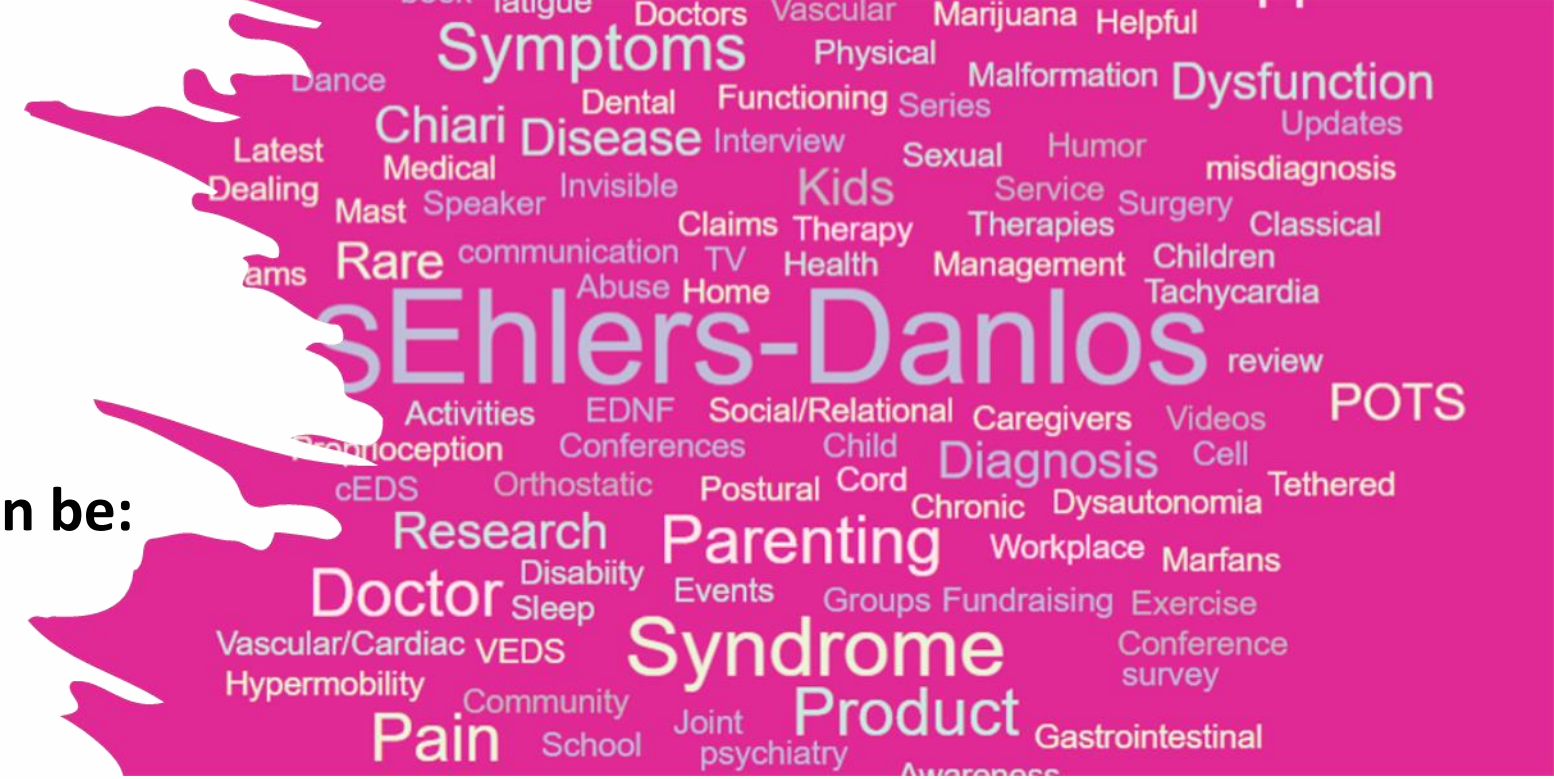


13 subtypes of Ehlers-Danlos Syndromes identified in the 2017 international classification of EDSs - 12 have a recognized, associated genetic mutation

Type of EDS (In order of estimated prevalence)	Approximate Prevalence	Associated Gene(s)	Affected Protein(s)	Inheritance Pattern	Distinguishing Features
Hypermobile EDS (hEDS)	1 in 3,100 – 5000	Unknown	Unknown	Autosomal Dominant	• Generalized joint hypermobility • Joint instability • Chronic Pain
Classical EDS (cEDS)	1 in 20,000 – 40,000	COL5A1	Type V collagen	Autosomal Dominant	• Skin fragility with extensive atrophic scarring • Very stretchy skin with velvety or doughy texture
		COL5A2	Type V collagen		
		COL1A1	Type I collagen		
Vascular EDS (vEDS)	1 in 100,000 – 200,000	COL3A1	Type III collagen	Autosomal Dominant	• Arterial fragility with aneurysm/dissection/rupture • Organ fragility and rupture • Extensive bruising • Pneumothorax
		COL1A2	Type I collagen		
Arthrochalasia EDS (aEDS)	Less than 1 in 1,000,000	COL1A1	Type I collagen	Autosomal Dominant	• Severe joint hypermobility • Congenital bilateral hip dislocation
		COL1A2	Type 1 collagen		
Brittle Cornea Syndrome (BCS)	Less than 1 in 1,000,000	ZNF469	ZNF469	Autosomal Recessive	• Severe problems with the cornea of the eye • Hearing loss
		PRDM5	PRDM5		
Cardiac-valvular EDS (cvEDS)	Less than 1 in 1,000,000	COL1A2	Type I collagen	Autosomal Recessive	• Severe heart valve insufficiency
Classical-like EDS (clEDS)	Less than 1 in 1,000,000	TNXB	Tenascin XB	Autosomal Recessive	• Stretchy, velvety skin without atrophic scarring • Foot deformities • Leg swelling
Dermatosparaxis EDS (dEDS)	Less than 1 in 1,000,000	ADAMTS2	ADAMTS-2	Autosomal Recessive	• Extreme skin fragility • Craniofacial features • Loose, excessive skin • Severe bruising • Short limbs

Kyphoscoliotic EDS (kEDS)	Less than 1 in 1,000,000	PLOD1	LH1	Autosomal Recessive	• Congenital/early-onset kyphoscoliosis • Congenital hypotonia
		FKBP14	FKBP22		
Musculocontractural EDS (mcEDS)	Less than 1 in 1,000,000	CHST14	D4ST1	Autosomal Recessive	• Congenital multiple contractures • Craniofacial features
		DSE	DSE		
Myopathic EDS (mEDS)	Less than 1 in 1,000,000	COL12A1	Type XII collagen	Autosomal Dominant or Recessive	• Congenital hypotonia • Proximal joint contractures
Periodontal EDS (pEDS)	Less than 1 in 1,000,000	C1R	C1r	Autosomal Dominant	• Severe, early-onset gum disease with tooth loss • Pretibial plaques (discoloration of shins)
		C1S	C1s		
Spondylodysplastic EDS (spEDS)	Less than 1 in 1,000,000	B4GALT7	β4GalT7	Autosomal Recessive	• Short stature • Muscle weakness • Limb bowing • Craniofacial features
		B3GALT6	β3GalT6		
		SLC39A13	ZIP13		

[Source www.ehlers-danlos.com/what-is-eds]



Compilations of these syndromes can be:

Chronic pain
Dysautonomia
Gastrointestinal dysmotility
Mast cell activation
Anxiety/depression
Infection chronic
Arterial rupture and organ perforation, with potentially life-threatening consequences

Hypermobile Ehlers-Danlos syndrome

Other Names: EDS III; EDS-HT; Ehlers-Danlos syndrome hypermobility type; Ehlers-Danlos syndrome type 3; Hypermobile EDS; hEDS

Most prevalent form of EDS (1:3-5K persons) - <200,000 people in the U.S. – Symptoms may start to appear throughout the lifespan – Proposed to be caused by a change in the genetic material (DNA) – hEDS currently has no identifiable associated gene – Higher prevalence ♀:♂

- Diagnosed by history & physical examination & classification using the Beighton & Brighton scores.
- There have been many ways proposed to differentiate between general hypermobility spectrum disorder(s) & hEDS including the severity of symptoms, immunity to local anaesthetics, multi-systemic involvement → no consensus how to differentiate between the diagnoses.
- Currently managed with early diagnosis to optimize the symptomatic management of patients and to prevent avoidable complications.
- Optimally patients should be treated and monitored by multidisciplinary teams in specialized centers, however the reality is that much of the preliminary diagnosis and treatment will begin in primary care.

BMJ Open. 2019 Nov 4;9(11):e031365. doi: 10.1136/bmjopen-2019-031365.

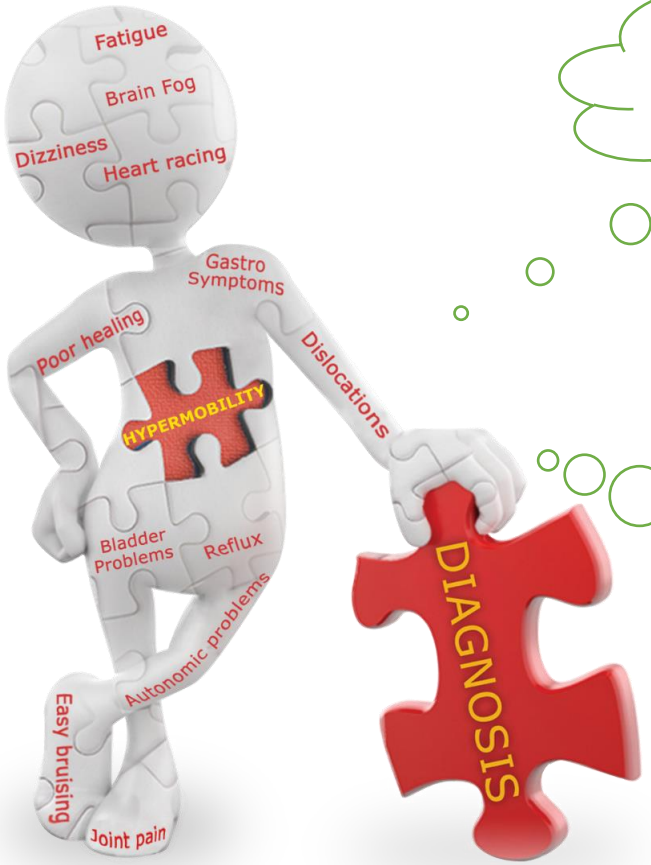
Diagnosed prevalence of Ehlers–Danlos syndrome and hypermobility spectrum disorder in Wales, UK: a national electronic cohort study and case–control comparison

Joanne C Demmler [1], Mark D Atkinson [2], Emma J Reinhold [3], Ernest Choy [4], Ronan A Lyons [2], Sinead T Brophy [2]

Reviewing over 30 years of Health System Data: To describe the epidemiology of diagnosed hypermobility spectrum disorder (HSD) and Ehlers-Danlos syndromes (EDS).

- We found 6021 individuals (men: 30%, women: 70%) with a diagnostic code of either EDS or JHS.
- EDS or JHS was not only associated with ↑ odds for other musculoskeletal diagnoses, but also with significantly higher odds of a diagnosis in other disease categories (e.g., mental health, nervous & digestive systems).
- Suggested that EDS/JHS had a prevalence closer to 1:500
- Historically been considered rare diseases only affecting the musculoskeletal system & soft tissues. These data demonstrate that both these assertions should be reconsidered.

What are the main symptoms of Hypermobile EDS?



Dislocations

Tummy problems

Stretchy skin

Easy bruising

Pain

Bendy joints

Fatigue

Feeling dizzy

CLINICAL FEATURES OF hEDS

Recurrent dislocation, subluxations or joint hypermobility (Joints)	Chronic musculoskeletal pain (Pain)	Autonomic dysfunction: postural hypotension, dizziness, Raynaud's disease, temperature in tolerance (Dysautonomia)	Tempo-mandibular joint dysfunction, caries (Teeth)	Easy bruising, poor wound healing (Skin)
Migraines (Headache)	Irritable bowel syndrome, celiac disease, GERD (GI)	Blurry vision (EYE)	Increased allergies, infections (Mast Cell)	Heavy menses, endometriosis, pelvic congestion (menses)

The **Brighton criteria** takes into account the **Beighton score** as well as other factors necessary to diagnose hEDS

To be diagnosed with EDS the patient must meet:

- Two major criteria
- One major and two minor criteria
- Four minor criteria
- Two minor criteria & a first-degree relative who has been diagnosed with hEDS

Brighton Criteria

- **Major Criteria**
  - Beighton score of ⩾4 *Figure 4*)
  - Arthralgia for longer than 3 months in 4 or more joints
- **Minor Criteria**
  - Beighton score of 1, 2, or 3 (*Figure\!s>4*)
  - Arthralgia (>3-month duration) in one to three joints or back pain (>3-month duration)or spondylosis, spndylolysis/spondylolisthesis
  - Dislocation or subluxation in more than one joint, or in one joint on more than one occasion
  - Three or more soft tissue lesions (eg, epicondylitis, tenosynovitis, bursitis)
  - Marfanoid habitus (tall, slim, span greater than height (>1.03 ratio), upper segment less than lower segment (<0.89 ratio), arachnodactyly)
  - Skin striae, hyperextensibility, thin skin, or abnormal scarring
  - Ocular signs: drooping eyelids, myopia, antimongoloid slant
  - Varicose veins, hernia, or uterine or rectal prolapse
  - Mitral valve prolapse
- **Requirement for Diagnosis**
  - Any one of the following:
    - — two major criteria
    - — one major plus two minor criteria
    - — four minor criteria
    - — two minor criteria and unequivocally affected first-degree relative in family history

The Ehlers Danlos Society

THE BEIGHTON SCORING SYSTEM

Measuring joint hypermobility

A. 5th FINGER / 'PINKIES'

Test **both sides**: Rest palm of the hand and forearm a **flat surface** with palm side down and fingers out straight.

Can the **fifth finger** be bent/lifted upwards at the knuckle to go back **beyond 90 degrees?**

If yes, add **one point** for each hand.

1 POINT FOR EACH HAND

B. THUMBS

Test **both sides**: With the arm out straight, the palm facing down, and the wrist then fully bent downward, can the thumb be pushed back to touch the forearm?

If yes, add **one point** for each thumb.

1 POINT FOR EACH THUMB

1 POINT FOR EACH LEG

D. KNEES

Test **both sides**: While standing, with knees locked (bent backwards as far as possible), does the lower part of either leg extend **more than 10 degrees forward?**

If yes, add **one point** for each side.

C. ELBOWS

Test **both sides**: With arms outstretched and palms facing upwards, does the elbow extend (bend too far) upwards **more than an extra 10 degrees** beyond a normal outstretched position?

If yes, add **one point** for each side.

1 POINT FOR EACH ARM

E. SPINE

Bend forward, can you place the palms of your hands **flat on the floor in front of your feet without bending your knees?**

If yes, **add one point.**

1 POINT

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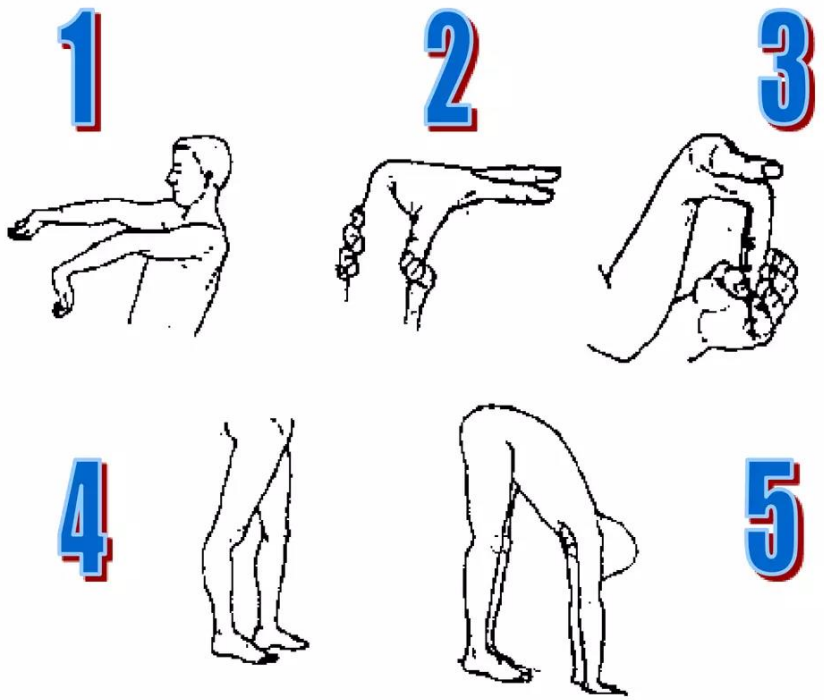
The Beighton Score

- A popular screening technique for hypermobility.
- Requires the performance of 9 maneuvers.
- A point is gained for each movement that the subject can positively perform.
- A **minimum** of 3 points to be considered mildly hypermobile.
- A **maximum** of 9 points would indicate extreme hypermobility.
- Is easy and quick to perform, even in large populations.
- Movements 1-4 are performed on both the right and left sides of the body.



Total = 9 possible 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.

Diagnosis: _____

v9

https://www.ehlers-danlos.com/wp-content/uploads/2017/05/hEDS-Dx-Criteria-checklist-1.pdf

ONGOING MANAGEMENT

- Echocardiogram
- DEXA (bone density scan)
- Vitamin D levels/Nutrition status
- Eye exam
- Physical therapy
- Pain control
- Mental wellness, coping

If available – refer to EDS specialist

TREATMENT: Multimodal/Multidisciplinary

- ✓ Symptom Management (pain)
  - medications/interventions
- ✓ Psychological Support
- ✓ Rehabilitation – Maintenance (PT/OT)
- ✓ Disease Management
- ✓ Nutrition
- ✓ Comorbid disease management
  - Cardiology
  - Rheumatology
  - Endocrinology
  - Geneticist
  - Gastroenterology
  - Pain Management
  - Orthopedics

PHARMACOLOGICAL TREATMENTS FOR PAIN

Acetaminophen, NSAIDS - control episodic and recurrent pain

Short course of steroids for acute flares of pain, +/- opioids sparingly

Muscle relaxants- use sparingly for cramps myalgias

Regular intake of magnesium- oral/topical (Epson salt baths)

Supplements - calcium, carnitine, coenzyme Q(10), glucosamine, magnesium, methyl sulphonyl methane, silica, vitamin C-D-B12

Probiotics (?) – promotion gut/microbiome health

Pregabalin, gabapentin- chronic pain with neuropathy

Antidepressants- TCA, SNRI

Considerations to pharmacological management

Mast cell activation syndrome, intra abdominal compression syndrome, disturb peristalsis have significant influences on oral drug therapy:

- Intolerance reactions to drug ingredients (formulations with rice starch preferred).
- Impaired absorption reduce bioavailability
- Alerted drug metabolism
- Start low and go slow with drug dosing
- Large scale randomized case control studies are still lacking for the use of drug therapy, conventional therapy approaches are generally adapted to individual needs.

Low-dose naltrexone

It can also help in those with mixed nociceptive and neuropathic pain and may even help with mood disorders.

Glial cell modulation

The research involving low-dose naltrexone within a specifically EDS population is severely lacking though, so this data is based on overlapping pain syndromes. Dosing remains variable, and long-term benefits are not understood.

Low-dose naltrexone trust: https://ldnresearchtrust.org/

LDN 2024 Dosing Information For Prescribers:
https://ldnresearchtrust.org/sites/default/files/2024-02/Dosing-Guide-2024_0.pdf

PAIN IN EDS

Physical Therapy

- Mainstay of treatment
- Splints, braces, massage therapies

Cognitive Behavioral Therapy

Surgery

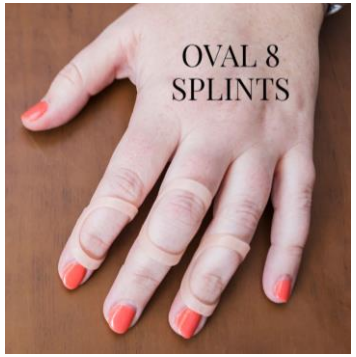
- Highly selective cases

Other Invasive Therapies

- Nerve blocks

Other

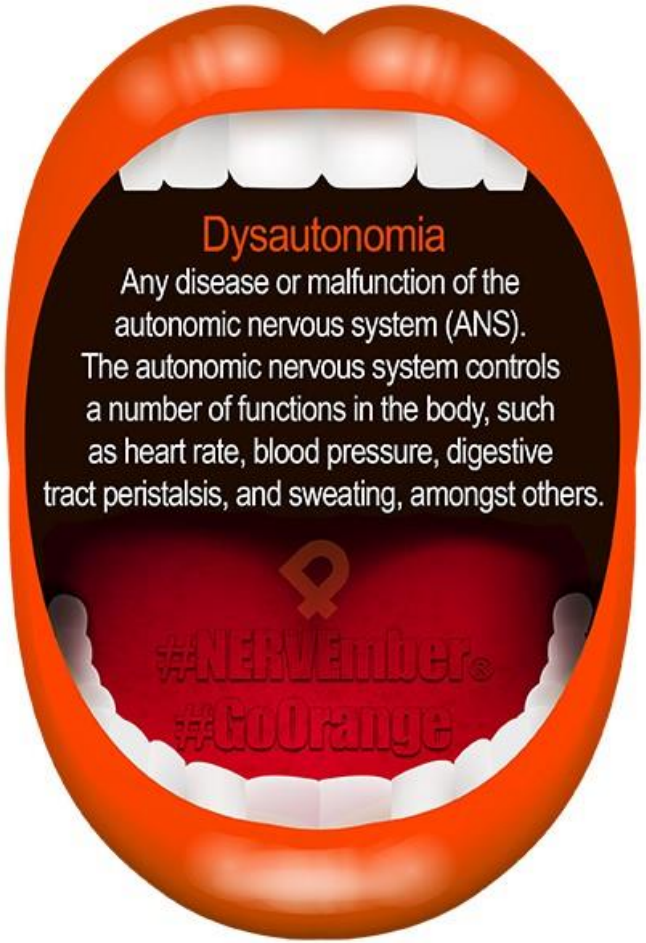
- Heated pools gentle Stretching
- Walking
- Hot and cold packs
- Yoga
- Relaxation therapy
- Ergonomic environment



DYSAUTONOMIA

Non-pharmacological measures

- Avoid triggers such as heat, prolonged standing/sitting, alcohol
- Increase fluid and salt intake
- Compression stockings
- Exercise
- Adequate sleep



Pharmacological measures

- Reduce heart rate - beta blockers
- Alpha agonists - midodrine
- Increase blood volume - fludrocortisone

GASTROINTESTINAL SYMPTOMS

Functional GI disorder - no well-validated management guidelines exist

Trial and error diet – microbiome – probiotics (?)

Diet low in FODMAP (fructose, oligosaccharides, disaccharides, monoamines, polyols)

Supplements - carnitine, coenzyme Q10, high dose vitamin C (1500 milligrams/day)

FATIGUE

Often receives little medical attention

Contribute significantly to burden of disease

Overwhelming sense of tiredness, lack of energy and feeling of exhaustion

Major determinant of disability which significantly affects quality of life

Patients with hEDS are most often severely fatigued

Severe fatigue is related to sleep disturbances, concentration problems, social functioning, pain

NEUROMUSCULAR INVOLVEMENT

Muscle hypertonia, rupture, pain

Due to direct effect of defect of extracellular matrix within muscle and nerves

Not because: people with EDS avoid exercise or have fear of dislocation & hyper extensibility of tendons

Patients with all types of EDS have mixed myopathic neurogenic features on EMG

Muscle biopsies show only mild changes

EDS in the classroom

- Emergency plan
- Avoiding injury: creating a safe environment with ergonomic furniture; locker heights; using elevators instead of stairs
- Preserving joints: avoid high impact, weight bearing or contact sports
- Emotional considerations
- Finger joints may be weak; may require additional time for test-taking; may need help with note-taking; pencils with good grips

A novel therapeutic strategy for Ehlers-Danlos syndrome based on nutritional supplements

The novel aspect of this proposal is based on:

- Increasing scientific evidence that nutrition may be a major factor in the pathogenesis of many disorders once thought to result from defective genes alone.
- Recognition that many of the symptoms associated w/EDS are also characteristic of nutritional deficiencies.
- Synergistic action within the body of appropriate combinations of nutritional supplements in promoting normal tissue function.

(Mantle, et al., 2005)

SYMPTOM	NUTRITIONAL SUPPLEMENT	DOSE
Joint injury/arthritis	Glucosamine	1500 mg/d
Scoliosis/osteoporosis/fracture	Vitamin C Calcium/Vitamin K	750 mg/d 500 mg/35μg/d
Muscle weakness/fibromyalgia/sciatica	Carnitine Coenzyme Q10	250 mg/d 100 mg/d
Fragile skin/bruising/poor healing	Vitamin C MSM plus silica	750 mg/d 1500 mg/3 mg/d
Bleeding Varicose veins	Vitamin C Pycnogenol	750 mg/d 80 mg/d
Raynaud's/ Peritonitis/Fatigue	Coenzyme Q10	100 mg/d
Inflammation/Pain	y-linolenic acid	240 mg/d

Nutritional Implications of Patients with Dysautonomia and Hypermobility Syndromes

Dysautonomia and hypermobility syndrome are two distinct but often overlapping clinical conditions that are recognized for their complex multiorgan system afflictions.

The purpose of this review is to investigate dietary strategies to reduce symptoms and augment quality of life in this growing patient population.

(Do, et al., 2021)

SYMPTOM	RECOMMENDATION
Diarrhea/flatulence/bloating (GI)	• FODMAP diet/gluten free diet/soluble fiber • Probiotic (Lactobacillus GG, Bifidiobacterium lactis) • SIBO treatment (rifaximin)
Constipation (GI)	• Fiber supplement • SIBO treatment, including methane positive
Normobiosis (GI)	• Probiotic rich foods (yogurt, kimchi, miso) • Lactobacillus, Bifidiobacterium, Clostridium, Streptococcus • Prebiotics (Inulin, Fructooligosaccharide, lactulose, milk oligosaccharides, beans, garlic, unripe bananas) • Supplements (5000 U vitamin D3, 750-1000 mg/d vitamin C, 1500 mg/d MSM, 3 mg/d silica, vitamin B12 & B1, antioxidants, fiber) • AVOID (alcohol, fructose, artificial sweeteners)

SYMPTOM	RECOMMENDATION
Orthostatic Hypotension (CV)	• Salt 6-9/10 g/d (AJC – 2017; ASH -2013) • Fluid 1.5-2L/2-3L (ASH – 2013, ESC – 2018) • Small frequent meals, room temperature
Osteoarticular /Joint (MSK)	• 1500 mg/d glucosamine • 1200 mg/d chondroitin • 228 mg/d manganese ascorbate
Musculoskeletal pain	• 250 mg/d carnitine • 100 mg/d coenzyme Q10 • 240 mg/d y-linolenic acid (anti-inflammatory)
Fatigue	Supplements (coenzyme Q10, magnesium, nicotinamide adenine dinucleotide (NADH), Alpha-lipoic acid)

Comprehensive Assessment of Nutrition and Dietary Influences in Hypermobile Ehlers-Danlos Syndrome-A Cross-sectional Study

Disorders of gut-brain interaction (DGBI) are common in patients with hypermobile Ehlers-Danlos syndrome/hypermobility spectrum disorder (hEDS/HSD).

Aim: To explore dietary behaviors and influencing factors in patients with hEDS/HSD.

680 participants - 62.1% altered their diet in the last year & 62.3% regularly skipped meals.

Altered diet was associated with the following:

- Reflux symptoms - Functional dyspepsia - Reported mast cell activation syndrome
- Fear of eating & low interest
- Approximately 31.7% of those who altered their diet required nutrition support

(Topan, et al., 2024)

Cognitive behavioral therapy (CBT)

- CBT for EDS can be helpful in managing psychological comorbidities impacting pain & impacted by pain.
- It is widely known that poor mental health impacts quality of life and often associated with pain syndromes.
- CBT & similar therapies can help address psychiatric comorbidities to improve QOL, pain severity, modulating pain catastrophizing & improving a patient's ability to manage pain experiences and pain interference connected to EDS or chronic pain.

In a recent study that divided hEDS patients by high & low anxiety, those in the high anxiety group reported more severe fatigue, ↑ rates of depressive symptoms, ↑ pain catastrophizing, ↑ somatosensory amplification, a lower overall functioning.

Addressing the **neurocognitive impacts of pain**, including perception, can help ↓ pain scores, pain interference. **This was especially helpful in combination with physical therapy.**

Physical Therapy/Occupational Therapy

Physical therapy (PT) & occupational therapy (OT) have been shown to be an effective way to ↓ pain & improve QOL for patients with EDS, in addition to minimizing kinesiophobia.

Joint instability & pain severity → many patients with EDS being wary to begin any intense training program, and even for those that do begin, there is a high dropout rate.

All PT/OT programs should be very carefully titrated & aimed at addressing ↓ pain & improving function & also regulating expectations → increasing autonomy. Fatigue should additionally be considered in training regimens, as common comorbidities, like POTS and dysautonomia, can amplify fatigue & pain.

Most PT/OT protocols in the current literature are 4–8 weeks → involve the use of integrated techniques → motor imagery & correcting poor proprioception.

Transcutaneous electrical nerve stimulation (TENS) is also helpful in alleviating pain severity. TENS works to dampen neuropathic pain via both central and peripheral pathways.

Along with exercise and adjuvants, orthoses (brace, taping, etc.) & energy conservation strategies can be used to help manage pain and joint displacement

- Trigger point injections can address musculoskeletal pain.

- Steroid injections in peripheral joints can help relieve the arthritic pain caused by joint degeneration, and the local administration of corticosteroids helps reduce the systemic side effects of steroids when compared to oral administration.

- Peripheral nerve blocks have also shown positive results in the EDS patient population, both with children and adults.

Laser therapy is a non-invasive & painless treatment modality (using non-ionizing light source) that can be beneficial for patients with EDS to treat soft tissue pain.

Diffuse soft tissue pain is prevalent in the EDS population due to the constant activation of muscles to counter joint laxity and repeated injury in strained tendons and ligaments.

It helps to ↑ cellular metabolism, renew protein synthesis, ↓ inflammation & improve microcirculation to injured tissue → accelerate the healing process. While there have been no studies looking at the efficacy of laser therapy on EDS patients specifically, it has been shown to be effective in various musculoskeletal disorders that EDS patients often suffer from.

Meta-analysis done by Song et al., the effectiveness of high-intensity laser therapy was evaluated across various musculoskeletal disorders → shown to significantly reduce pain & disability scores not only for musculoskeletal disorders overall, but also for different treatment areas.

(Song, et al., 2020; Ezzati, et al., 2020)

A 40-year-old Caucasian woman with history of long-standing joint pain & chronic fatigue syndrome presented with new-onset right shoulder pain.

The pain began 1-month prior, with a grinding quality and the sensation of joint “displacement” when she leaned on her right side. No new trauma or identified inciting event.

On review of systems, it was found that she has chronic headaches and joint pain, and “fragile skin”.

She states that she remembers her aches and pain beginning around pre-adolescence.

Contributing past medical history:

Musculoskeletal symptoms → TMJ disorder, chronic joint and muscle pain, low back pain & repetitive motion injuries. Frequent sprained ankles, which happened seemingly with no inciting event. She reported easy bruising.

Cardiovascular history → diagnosis of orthostatic hypotension in her youth, which had never been medicated; she continues to experience dizziness and lightheadedness upon standing.

Gastrointestinal history → irritable bowel syndrome (IBS) and frequent nausea. She is being treated for deficiencies of vitamin D, for which she is taking supplements, and B12, for which she is receiving subcutaneous injections.

She recently developed various chemical sensitivities but reported no medication allergies.

In addition → diabetes mellitus type 2, hyperlipidemia, and depression.

Family history was noncontributory with the exception of her daughter, who is currently being tested for POTS.

Physical examination:

The musculoskeletal examination revealed normal strength in all extremities, with pain to palpation over the rotator cuff.

Joints were examined for hypermobility using the Beighton scale criteria. The patient scored a 5/9: bilateral fifth digit passively extended to 90°, the left thumb was opposable to the forearm (examination of the right thumb was deferred secondary to prior arthritis pain), and bilateral elbow extension past 10°.

She was unable to palm the floor but expressed that she would have been able to do so easily when she was younger prior to weight gain.

Integumentary examination revealed soft, velvety skin with normal extensibility. Upon drawing a tongue depressor across her forearm, an erythematous wheal appeared in under 30 seconds.

Would you feel comfortable making the clinical diagnosis of Ehlers– Danlos syndrome hypermobility type?

History & physical examination findings:

- Beighton score of 5/9
- Velvety, doughy skin
- Patient's history of widespread joint pain, spontaneous joint injury & TMJ disorder

→ Support a diagnosis of hEDS.

Autonomic dysfunction:

- Postural hypotension
- IBS

→ Considered underdiagnosed comorbidities of hEDS

Mast cell activation disorders (dermatographia & chemical sensitivities) → possible connection to hEDS

Further Discussion:

The major diagnostic challenge is in recognizing the underlying diagnosis that connected her wide and complex history.

Co-morbid: diabetes, arthritis, and depression – as well as being overweight, her joint pain had largely been dismissed.

Follow up:

- Cardiology for an echo to rule out vascular involvement, in particular aortic root dilation.
- Maxillofacial and Oral Surgery for TMJ pain control
- PM&R for joint pain control and physical assessment.
- Physical therapy and pharmacotherapy.

A 14-year-old male presented to an outpatient headache clinic with a 5-year history of headache, which had become daily over the past 3 months and awakened him in the middle of the night.

Characteristics including photophobia, phonophobia, nausea, vomiting but denied visual changes, numbness, tingling weakness, or focal deficits. He complains of 3-4 migraine headaches a week. In addition, he complains of dizziness, which typically occurred upon standing.

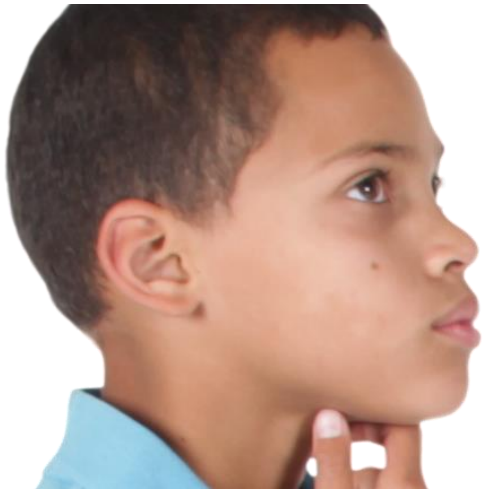
Past history also revealed

- Chronic musculoskeletal pain
- Syncope
- Fatigue
- Joint hypermobility
- Easy bruising

Where to start?

Do you need more history? Referrals? Ready to make a diagnosis, start treatment?

More History:



- The patient had a history of developmental delay, he did not walk independently until 2 years of age. Now is developmentally appropriate and is an average student in the 8th grade.

- There was a strong family history of mental health disorders. The patient had previously been referred to a psychiatrist and was subsequently diagnosed with depression & anxiety, but medication intervention had not yet been initiated.

- Plays soccer and baseball. Has suffered several ankle sprains over the past 2 years. Daily habits included at least 8-9 h of sleep during the school week but she reported nighttime awakenings, daytime sleepiness, and sleeping more hours on the weekends. Tends to eat “on the run” or skip meals during the week.

Objective:

On general exam, he showed increased elasticity of his skin, joint laxity of his extremities but no atrophic scarring. Neurological examination was unremarkable.

Recent lab work, including a complete blood count (CBC/diff), was unremarkable. X-rays cervical, thoracic, and lumbar spine, which were unremarkable.

Due to a recent history of increased headache frequency and awakening in the middle of the night with headache, he underwent a MRI brain.

- Unremarkable

He also revealed a history of snoring, nighttime awakenings, and daytime sleepiness.

- A polysomnography was ordered and demonstrated mild obstructive sleep apnea.

Any other tests, labs, objective information that you might want?

Referrals:

Rheumatology → diagnosed him with hypermobility of her joints.

Cardiology → diagnosed him with vasovagal syncope and recommended a hyperhydration protocol.

Psychiatry → and was subsequently diagnosed with depression and anxiety but medication intervention had not yet been initiated.

Neurology → medication intervention for headache was deferred and a trial of Mg was started.

Given the above history, he was referred to Genetics and, based on history and examination, the diagnosis of mild classic hEDS was confirmed.

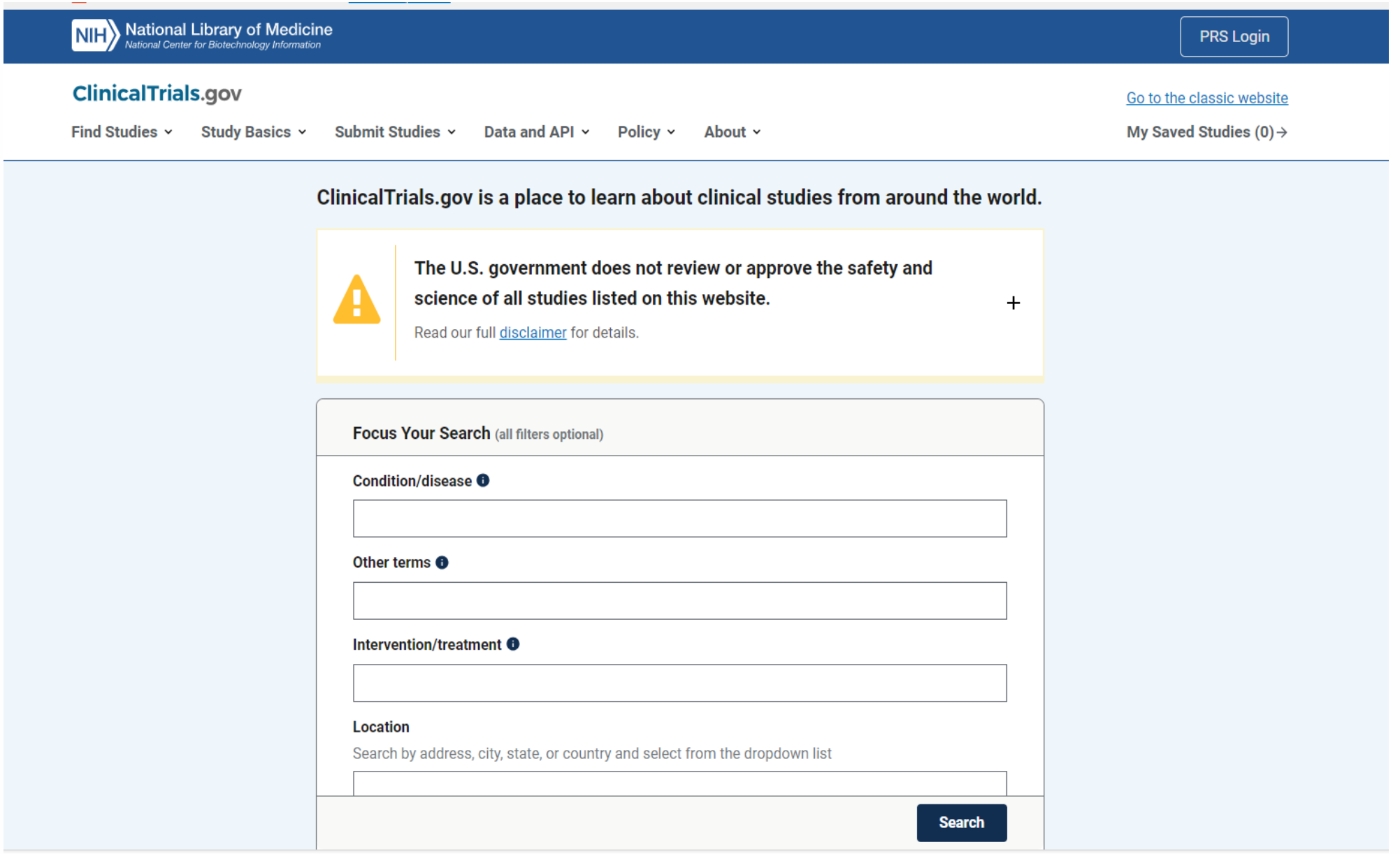
Treatment:

Acute – manage current complaints

- Poor sleep
- Headache/migraine
- Anxiety
- Ankle sprains

Chronic – prevent future injury, illness

- CV compromise, syncope
- Depression
- MSK injury
- Chronic pain



CANP 46TH ANNUAL EDUCATIONAL CONFERENCE

The DICE EDS and HSD Global Registry

https://www.ehlers-danlos.com/eds-global-registry/

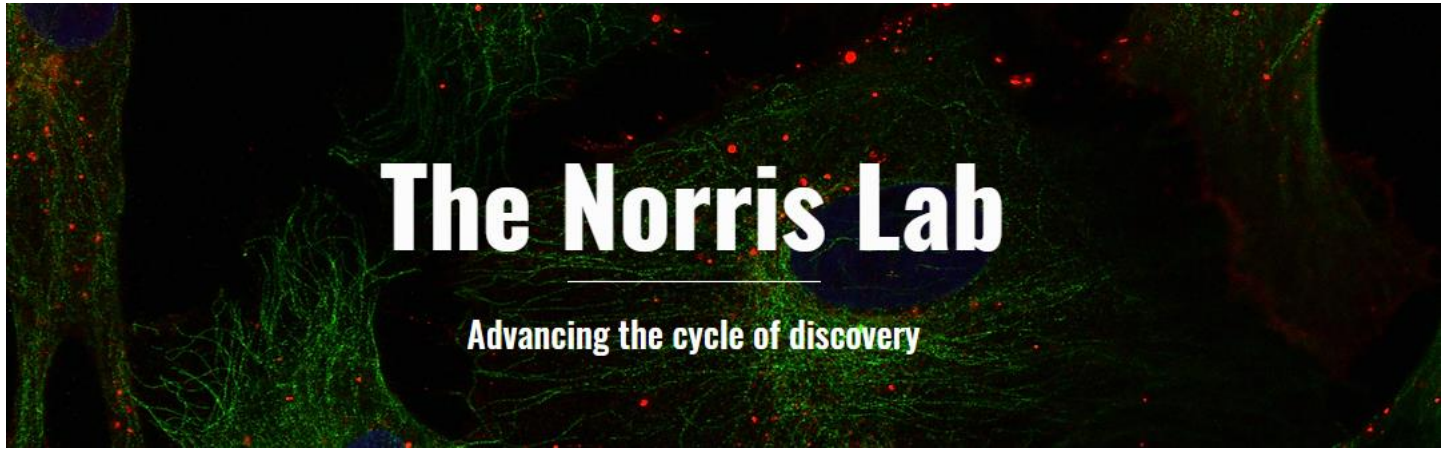
MUSC
Medical University of South Carolina

College of Medicine

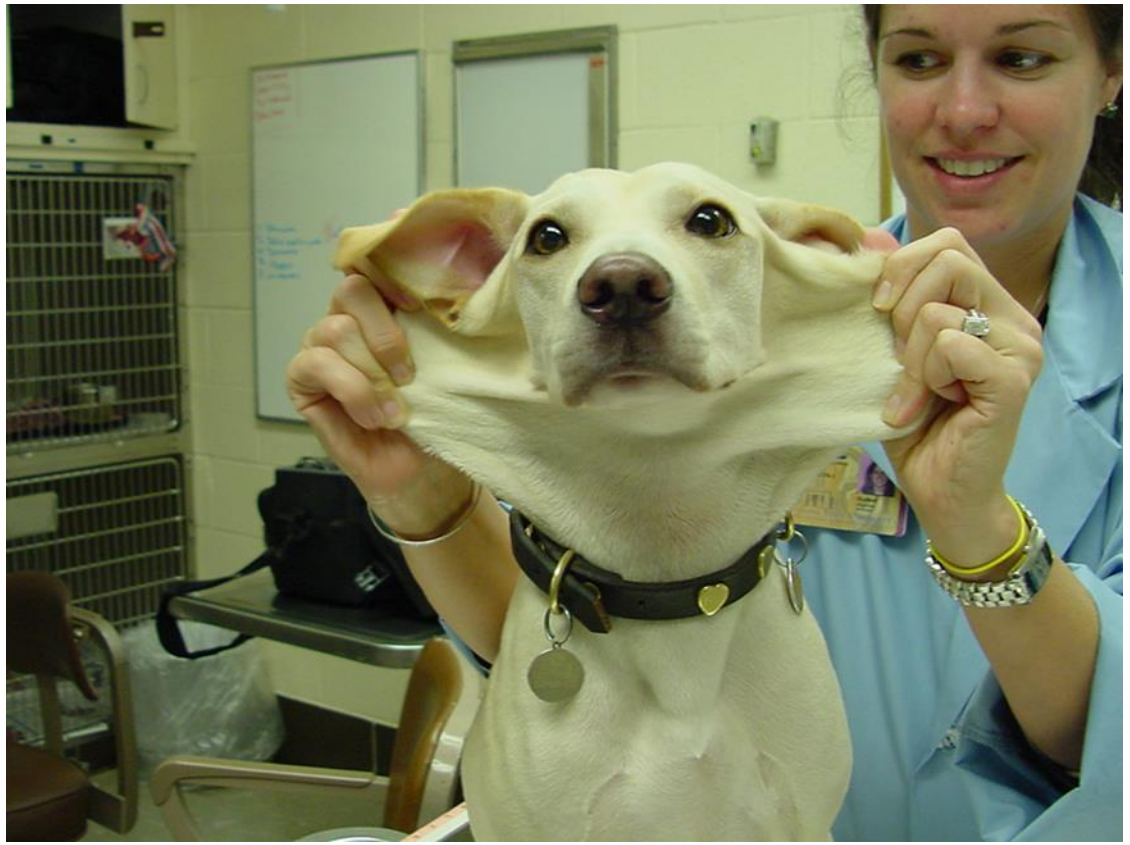
https://www.thenorrislab.com/eds

Ehlers-Danlos Syndrome Research

Deciphering the Genetic and Molecular Foundations of EDS



Thank you for listening!



Fun Fact!

Dogs can get EDS too!

A main symptom for them is extremely stretchy skin!

They have to be looked after too

Resources:

EDS ECHO Programs & Courses for Healthcare Professionals
https://www.ehlers-danlos.com/eds-echo-healthcare-professionals/

Ehlers-Danlos News - https://ehlersdanlosnews.com/

National Organization for Rare Disorders - https://rarediseases.org/

Ehlers-Danlos Syndrome (EDS) Algorithm and Resources for Primary Care/Mountain States Regional Genetics Network - https://www.mountainstatesgenetics.org/projects/eds-algorithm/

Resources:

Western States Regional Genetics Network - https://www.westernstatesgenetics.org/

The Ehlers Danlos Society - https://www.ehlers-danlos.com/
https://www.ehlers-danlos.com/healthcare-professionals-directory/

Ehlers-Danlos Support UK – https://www.ehlers-danlos.org/

EDS Awareness - https://www.chronicpainpartners.com/

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