Ehlers-Danlos Syndrome (EDS) (also known as Cutis hyperelastica) is a group of inherited connective tissue disorders caused by defects in the synthesis of collagen. It is named after two physicians who identified it at the turn of the 20th century. EDS affects men and women of all racial and ethnic backgrounds.

Collagen is the most abundant protein in the human body, which acts as a "glue" in the body, adding strength and elasticity to connective tissue. It provides structural strength in tissues, including heart and blood vessels, eyes and skin, cartilage and bone. When muscles, ligaments, tendons and even large organs are built with structurally defective collagen, there can be system weakness and instability evident throughout the body.

Currently, there are six distinct types of EDS identified. All share joint laxity, soft skin, easy bruising, and some systemic manifestations. Joint laxity results in widespread chronic pain, joint instability and spontaneous subluxations/dislocations. Each type is thought to involve a unique defect in connective tissue, although not all of the genes responsible for causing EDS have been identified.

Although the type of EDS runs true in a family, the symptoms of individual family members can vary so widely from each other that EDS is often misdiagnosed or ignored, and is therefore more frequent than previously thought. Hypermobility (HEDS) is the most common type with an estimated incidence of 1 in 2,500, followed by Classical type (CEDS) with an estimated incidence of 1 in 20,000, then Vascular type (VEDS) with an estimated incidence of 1 in 100,000, then Kyphoscoliosis type, also with an estimated incidence of 1 in 100,000. The remaining types are quite rare. This tool focuses mostly on the Hypermobility type, but also contains some information and statistics on the Classical and Vascular types and a little on the Kyphoscoliosis type.

The diagnosis of Hypermobility type EDS is based entirely on clinical evaluation and family history. In most individuals with HEDS, the gene in which mutation is causative is unknown and unmapped. Haploinsufficiency of tenascin-X has been associated with HEDS in a small subset of affected individuals. HEDS is inherited in an autosomal dominant manner, meaning children have a 50% chance of inheriting it from an affected parent. The proportion of de novo (spontaneous) mutations is unknown.

Since its early definition as a Hereditary Connective Tissue Disorder (HCTD) with predominant rheumatologic manifestations, HEDS is emerging as a widespread disorder with reverberations in practically all organs and systems. Although most complications are not life-threatening and many patients have a nearly intact life span, the pervasive nature of the disorder often makes their quality of life poor and restricted by worsening disability. The spectrum of clinical implications of lax joints even outside rare and well-defined HCTDs seems to be wider than previously expected, in contrast to the quaint adage of considering Joint Hypermobility (JHM) a benign, asymptomatic trait. HEDS patients often “migrate” from one specialist to another referring every time with a different complaint.

At the moment, the long-term treatment of HEDS is largely unsuccessful in terms of amelioration of symptoms. In fact, after years of treatment cycles and follow-up evaluations, many patients still refer the complaints reported at first evaluation. This anticipates that, actually, the best result of all practitioners' efforts is to stabilize symptoms with short periods of complete/partial relief.
Musculoskeletal pain is a major determinant for deterioration of quality of life in HEDS. Although it usually starts as occasional/recurrent joint pain facilitated/triggered by joint instability (e.g., dislocations and sprains), subsequently it becomes pathogenically heterogeneous usually manifesting in the form of widespread myalgias and arthralgias and often with neuropathic features. Pain chronicization and resistance to treatment are the most relevant features influencing prognosis. The best management program should include drugs, physical therapy, cognitive-behavioral therapy, and adherence to a series of lifestyle recommendations. For this reason, while occasional and low-to-moderate recurrent pain may be treated in an outpatient setting by a specialist (e.g., clinical geneticist, rheumatologist, physiatrist, or general practitioner), management of chronic or highly disabling recurrent musculoskeletal pain in HEDS usually needs a multidisciplinary approach.

The diagnosis of Classical type EDS is established by family history and clinical examination. At least 50% of individuals with Classical type have an identifiable mutation in \( \text{COL5A1} \) or \( \text{COL5A2} \), the genes encoding type V collagen. CEDS is inherited in an autosomal dominant manner. Approximately 50% of individuals with CEDS have a \textit{de novo} disease-causing mutation.

The diagnosis of Vascular type EDS is based on clinical findings and confirmed by identification of a causative mutation in \( \text{COL3A1} \), the only gene in which mutations are known to cause VEDS. Sequence analysis detects 98% of mutations. VEDS is inherited in an autosomal dominant manner. Approximately 50% of individuals with VEDS have a \textit{de novo} disease-causing mutation.

There are some doctors who refuse to diagnose EDS because it's so rare—this is just bad logic; of course it's rare if no one diagnoses it because it's rare. Rarity of a disorder has nothing to do with whether or not it applies to you personally. You will find doctors who don't want to diagnose it because it's not curable. Remind them that even though it has no cure, the symptoms can be treated, and knowing you have a type of EDS gives you and your medical team some idea of where problems might come from and why they're happening; if there ever is a cure, at least you'll all know to use it; and the more of us who are diagnosed, the more likely it is EDS will get the attention we all need and the more likely researchers will work on finding a cure. Even knowing what type you have, your own case of EDS will be your own case; while knowing what might happen is helpful, you'll probably have only a subset of symptoms and not the whole set.
**Diagnosis of HEDS:** The Beighton scale and the newer Brighton scale are used to diagnose Ehlers-Danlos Syndrome Hypermobility Type.

Beighton 9-point scoring system for joint hypermobility (1 point for right, 1 point for left). Based on ability to perform a series of maneuvers:

<table>
<thead>
<tr>
<th>1. Passive dorsiflexion of the little fingers beyond 90 degrees</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Right" /></td>
<td><img src="image2" alt="Left" /></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Passive apposition of the thumbs to the flexor aspect of the forearm</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="Right" /></td>
<td><img src="image4" alt="Left" /></td>
</tr>
</tbody>
</table>
3. **Hyperextension of elbows beyond 10 degrees**

<table>
<thead>
<tr>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
</table>

4. **Hyperextension of the knees beyond 10 degrees**

<table>
<thead>
<tr>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
</table>
5. Forward flexion of the trunk with knees fully extended so that the palms of the hand rest flat on the floor (place the hands flat on the floor with the knees fully extended)

A score of 5/9 or higher is usually taken into consideration to indicate generalized hypermobility. Hypermobility should also be sought in joints outside the 5 sites that form part of the Beighton scoring system, as each hypermobile joint identified will add evidence of joint hypermobility.
Joint hypermobility can also be determined indirectly by using the following 5 question questionnaire. An answer in the affirmative to 2 or more questions suggests hypermobility with a sensitivity of 80% to 85% and a specificity of 80% to 90%. Answer Y/N

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Can you place your hands flat on the floor without bending your knees or could you ever?</td>
<td></td>
</tr>
<tr>
<td>2. Can you bend your thumb to touch your forearm or could you ever?</td>
<td></td>
</tr>
<tr>
<td>3. As a child did you amuse your friends by contorting your body into strange shapes? (cannot do the splits though)</td>
<td></td>
</tr>
<tr>
<td>4. As a child or teenager did your shoulder or kneecap dislocate on more than one occasion</td>
<td></td>
</tr>
<tr>
<td>5. Do you consider yourself double-jointed</td>
<td></td>
</tr>
</tbody>
</table>

**Brighton criteria**: take into account your Beighton score, but also consider other symptoms, such as joint pain and dislocated joints, and how long you have had them. There are major and minor Brighton criteria. Joint hypermobility may be diagnosed if you have:

- 2 major criteria
- 1 major criteria and 2 minor criteria
- 4 minor criteria
- 2 minor criteria and a first-degree relative who has been diagnosed

**Major criteria:**
- Having a Beighton score of 4 or more, either now or in the past
- Having joint pain for longer than 3 months in 4 or more joints

**Minor criteria:**
- Having a Beighton score of 1 to 3, or having a Beighton score of 0 to 3 if you are over 50 years of age
- Joint pain for longer than 3 months in 1 to 3 joints, or back pain longer than 3 months, or spondylosis (spinal arthritis) or spondylolisthesis (where one small bone in your spine slips forward over another bone)
- Dislocating, or subluxing (partially dislocating) more than 1 joint or the same joint more than once
- Having 3 or more injuries to your soft tissues, such as tenosynovitis (inflammation of the protective sheath around a tendon), bursitis (inflammation of a fluid-filled sac in a joint), or epicondylitis (tennis or golfer’s elbow)
- Abnormal skin: striae, hyperextensibility, thin skin, papyraceous scarring
- Eye signs: drooping eyelids or myopia or antimongoloid slant
- Varicose veins or hernia or uterine/rectal prolapse
- Having particular physical characteristics called Marfanoid habitus, which include being tall and slim and having long, slim fingers
  - arm span/height ratio > 1.03
  - lower limb length (floor to pubis) to upper body (pubis to crown ratio) > 0.89
  - foot length (heel to first toe) to height ratio > 0.15
---hand length (wrist crease to third finger) to height ratio >0.1
---highly arched palate with dental crowding
---scoliosis
---arachnodactyly (long, slim fingers) judged by positive Walker wrist sign and Steinberg thumb

Sign (see pictures below)

Walker wrist sign (able to wrap the thumb and fifth finger of one hand around the opposite wrist such that the nail beds of the digits overlap with each other)

Steinberg thumb sign – positive if the adducted thumb across the palm projects beyond the ulnar border in the clenched hand

Standards for Evaluating Range of Motion (ROM) of Adults’ Joints

<table>
<thead>
<tr>
<th>Movement</th>
<th>Maximal ROM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder elevation through flexion</td>
<td>180°</td>
</tr>
<tr>
<td>Elbow extension</td>
<td>190°-195°</td>
</tr>
<tr>
<td>Elbow pronation-supination</td>
<td>170° (80° in supination &amp; 90° in pronation)</td>
</tr>
<tr>
<td>Wrist flexion</td>
<td>80°</td>
</tr>
<tr>
<td>Wrist extension</td>
<td>70°</td>
</tr>
<tr>
<td>Wrist ulnar deviation</td>
<td>30°</td>
</tr>
<tr>
<td>Wrist radial deviation</td>
<td>20°</td>
</tr>
<tr>
<td>2^{nd} finger MCP joint extension</td>
<td>45°</td>
</tr>
</tbody>
</table>
PIP and DIP joint extension 0°
Hip abduction with leg extended 45°
 Hip adduction with leg extended 30°
Knee extension 180°-190°
Ankle dorsiflexion 20°
Ankle plantar flexion 50°
1st toe MTP joint extension 70°
Mandible depression 35-50mm
Mandible protrusion 3-7mm
Mandible lateral deviation 10-15mm
Neck rotation 11cm
Neck flexion 45°
Neck extension 45°
Neck lateral flexion 45°
Thoracolumbar spine lateral flexion 35°

1The lower end for men, the upper end for women
2MCP: metacarpophalangeal
3PIP: proximal interphalangeal, DIP: distal interphalangeal
4MTP: metatarsophalangeal
5From the tip of the chin to the lateral aspect of the acromion process

Joint/Bone Manifestations of EDS

- Cracking or popping joints feels like it relieves pressure
- Tendonitis
- Joint dislocation/subluxation, especially of the shoulder, patella and temporomandibular joints, which may occur spontaneously and are often reduced by the EDSer
- Muscle spasm
- Bursitis (inflammation of a fluid-filled sac in a joint), especially greater trochanteric bursitis in those with iliotibial band syndrome
- Bunion with joint fluid leak (ganglion cyst/pseudo tumor)
- Tenosynovitis (inflammation of the protective sheath around a tendon)
- Epicondylitis (tennis elbow & golfer’s elbow)
- Early onset osteoarthritis (OA), possibly because of chronic joint instability resulting in increased mechanical stress
- Early onset degenerative joint disease (DJD)
- Hypermobile joints
- Unstable joints that are prone to: sprain, dislocation, subluxation and hyperextension
- Talipes equinovarus (clubfoot) (12% of Vascular)
- Congenital dislocation of the hips (3% of Vascular)
- Appear klutzy
- Difficulty or pain walking
- Difficulty writing, silver ring splints help
- Cervical (neck) instability; may have trouble holding up your head
- Fluid effusion in the knees, ankles & elbows (primarily Classical or Kyphoscoliosis)
- History of delayed walking
- Omission of crawling and substitution of bottom-shuffling
Spontaneous easy reduction or replacement of the finger digits and shoulders
Joint and/or muscle pain as a child (growing pains)
Carpal tunnel syndrome
Pes planus (flat footed) with or without over pronation
Metatarsus adductus (foot deformity that causes the forefoot to turn inward)

Musculoskeletal pain is early in onset, chronic, and may be debilitating. The anatomical distribution is wide and tender points can sometimes be elicited. A tender point is defined as an area that, when palpated with the thumb or two or three fingers will be painful at a pressure of 4 kg or less. (Hypermobility)
Weak muscle tone (hypotonia) in infancy, which can delay the development of gross motor skills such as sitting, standing, and walking (Kyphoscoliosis)
Osteopenia (low bone density)
Stretchy ligaments and tendons
Tearing of tendons or muscles
Sprains or twisting of the ankles

Swan neck deformity of the fingers

Deformities of the spine, such as: Scoliosis (curvature of the spine, shown below), Kyphosis (a thoracic hump), Spondylosis (degenerative spinal changes)

Atlantoaxial subluxation (subluxation of the first two cervical vertebrae)
Disc herniation and disc degeneration
All joint sites can be subject to joint instability, including the extremities, vertebral column, costo-vertebral and costo-sternal joints, clavicular articulations and temporomandibular joints
Trendelenburg's sign (a gait adopted by someone with an absent or weakened hip abductor mechanism)
Buckling or “giving out” of the knees
Iliotibial band syndrome or “snapping hip” is a common symptom, often perceived by the individual as hip joint instability
Osteoporosis – bone mineral density in Hypermobility and Classical types may be reduced by up to 0.9 SD compared to healthy controls, even in young adulthood
Platyspondyly (Spondylocheirodysplasia)
Pectus excavatum (the sternum sinks inward)
Thoracic asymmetry
Genu recurvatum (backward curvature/hyperextension of the knee)
Skin manifestations

- Capillary fragility causes increased tendency to and delayed resolution of ecchymoses. (Bruise easily and bruises take a long time to go away).
- Severe bruising (50% of Kyphoscoliosis)
- Atrophic scarring (50% Kyphoscoliosis)
- Subcutaneous spheroids are small spherical hard bodies, frequently mobile and palpable on the forearms and shins. Spheroids may be calcified and detectable radiologically. (Classical)
- Fragile skin that tears easily
- Chillblains (Classical)
- Elastosis perforans serpiginosa (Classical)
- Skin striae (stretch marks)
- Soft, velvety skin that is fragile and sometimes highly elastic (Classical)

Piezogenic papules (small, soft lumps that appear on the side of the heel when the person is standing but which disappear when the foot is elevated) (Classical)

Skin that sags and wrinkles (Dermatosparaxis)

Skin hyperextensibility

Wounds that split open with little bleeding & leave scars that widen over time to create characteristic shallow “cigarette paper” scars (Classical)

Surgical incisions present problems with healing, with stitching skin sometimes described as "like sewing butter;” often requires sutures closer together and left in for longer than usual

Molluscoid pseudotumors (small spongy tumors consisting of fat surrounded by a fibrous capsule found over scars and pressure points) (Classical)

Thin translucent skin where blood vessels below are clearly visible (Classical & Vascular)
Delayed wound healing
Smoothed out finger pads (longitudinal wrinkles over finger pads)
Acrogeria (an aged appearance to the extremities, particularly the hands) (Vascular)
Dewlaps (folds of skin hanging from the neck)
Lavender macules over old insect bites
Aged facial appearance
Tight skin around lower face (Vascular)
Keratosis pilaris (KP) – excess keratin forms hard plugs that surround and entrap the hair follicles in the pore, which may contain an ingrown hair that has coiled. Characterized by rough, slightly red bumps on the skin, usually on the back and outer sides of the arm. It can also occur on the thighs, hands, tops of legs, sides, buttocks and face.
Double fold of skin picked up on the dorsum of the hand is frequently felt to be thin

**Autonomic Manifestations**
Dysautonomia
Orthostatic intolerance (74% of EDSers)
Postural Orthostatic Tachycardia Syndrome (POTS) (heart rate that increases 30 beats or more per minute upon standing) (41% of EDSers)
Insomnia, non-restorative sleep, frequent awakenings during the night
Daytime sleepiness/severe fatigue (84% Hypermobility and 69% Classical)
Hyper startle reflex
Raynaud's phenomenon
Reactive hypoglycemia
Feelings of panic/being overwhelmed
Over-response to physical and emotional stresses
Lightheadedness
Severe fatigue (84% Hypermobility, 69% Classical; 57% reported fatigue as one of their 3 most important symptoms. Fatigue has greater impact than pain on daily function).
Carpal tunnel syndrome
Hyperhydrosis (excessive sweating)
Low body temperatures; trouble controlling body temperatures when exposed to heat or cold (your thermostat is broken)
Palmoplantar hyperhidrosis with body hypohidrosis (sweaty palms & feet with less sweat on body)
Overproduction of adrenaline
Mast cell activation disorders (abnormal accumulation of tissue mast cells in one or more organ systems) –symptoms can include: weight loss, pain, nausea, vomiting, diarrhea with abdominal pain, uterine cramps or bleeding, shortness of breath, dysphonia, ECG alterations that can include ischemic ST-waves, arrhythmias and atrial fibrillations, peptic ulcer disease, severe bone pain, urticaria, angioedema, impaired level of consciousness, a sense of impending doom, pruritus, flushing, severe headache, malaise, fatigue, syncope, hypotensive shock, anaphylaxis

Gastrointestinal Manifestations (Functional bowel disorders affect 84% of EDSers)
Frequent Bloating/Gas
Chronic/recurrent gastritis (48% of Hypermobility)
Reflux and GERD (74% of Hypermobility, 68.7% of EDSers)
Irritable Bowel Syndrome (IBS) may manifest with diarrhea and/or constipation, associated with abdominal cramping and rectal mucus (48% of EDSers)
Diverticulitis
Gastroparesis (partial paralysis of the stomach)
Hiatus hernia
Megacolon and rectal prolapse, primarily in childhood
Tissue extensibility and laxity can cause lack of contraction of the stomach, causing food to not move down into the intestines
Chronic (slow transit) constipation
Early satiety
Crohn’s disease
Fecal incontinence

Delayed gastric emptying

Recurrent abdominal pain (68% of Hypermobility)

Constipation/diarrhea (72% of Hypermobility, 36% of EDSers)

Rectal evacuatory dysfunction

Rectal prolapse (the rectum fall from its normal position, sometimes protruding from the anus)

Celiac disease

Visceroptosis [a prolapse or a sinking of the abdominal viscera (internal organs) below their natural position]

Salt cravings

Biliary tract anomalies

Cholecystitis (inflammation of the gallbladder) and decreased gallbladder function
Cardiovascular Manifestations

- 20% of Vascular EDSers experience a major vascular event or rupture of an internal organ by age 20 years, and 80% by age 40 years. Vascular EDSers have a shortened life span with a median age of death of 48 years.

- Incompetent heart valves

- Aortic root dilation (12% of Hypermobility and 6% of Classical)

- Aortic dissection (Classical & Hypermobility have an increased risk)

- Bicuspid aortic valve

- Arteries including the aorta are very fragile and can rupture (Vascular)

- Difficult for a medical professional to "feel" your pulse

- Blood pressure problems/low blood pressure

- Intracranial vascular abnormalities (also listed under neurological manifestations)

- Drawing blood/placing an IV may require multiple attempts

- Tachycardia

- Varicose veins

- Tendency to prolonged bleeding in spite of normal coagulation status

- Mitral valve prolapse (6% of Hypermobility and Classical)

- Tricuspid insufficiency (Classical)

- Proximal aortic dilation (uncommon presentation)

- Atypical chest pain

- Palpitations at rest or on exertion

- Cardiac septal defects

- Holter monitoring usually shows normal sinus rhythm, but sometimes reveals premature atrial complexes or paroxysmal supraventricular tachycardia

- Mild mitral, tricuspid and aortic valve regurgitation (25% of Classical and Hypermobility)

- Acrocyanosis (Hypermobility and Classical)

- Aneurysms of descending aorta or pulmonary artery

- Renal vein thrombosis (blood clot in the renal vein)

- Risk for bacterial endocarditis

Pulmonary Manifestations

- Increased rate of asthmatic symptoms and atopy, often a side effect of GERD

- Reduced vital capacity

- Spontaneous pneumothorax (air in pleural cavity causes lung collapse)

- Emphysema (over inflation of the alveoli, causing decreased lung function and breathlessness)

- Anesthesia risks

Oral/Dental Manifestations

- Cavity prone

- High palate

- Crowded baby and adult teeth

- Smaller than normal teeth

- Increased bleeding from anywhere in the oral cavity due to the fragility of tissues
Pre-molar and molar teeth often have high cusps and deep fissures with root problems, and enamel hypoplasia can cause decay and possible early extractions. Sometimes teeth actually crumble when losing the enamel.

TMD (temporomandibular joint pain and clicking) (>70% of Hypermobility) Often if in a dental chair with your mouth open for an extended period of time, the joint will repeatedly sublux.
---can mimic an earache
---tinnitus (ringing in the ears)
---hearing loss
---itching in ear
---articular locks (jaw locks up)
---myofascial pain

Early onset periodontitis/gingivitis

Bone/tooth density problems

Gorlin sign (ability to touch tongue to tip of nose)--10% of general population vs. 50% of EDSers

Juvenile periodontal disease (Classical)

Lidocaine (a local anesthetic used during dental procedures) often works poorly or not at all with EDS patients.

Always feeling like there is a lump in your throat when swallowing, and often having other swallowing and voice problems.

Laryngitis

Xerostomia (dry mouth)

Oropharyngeal dysphagia (difficulty swallowing)

Mandibular prominence

Dental malocclusion (teeth not aligned properly)

Mandibular prognathism/underbite (the lower jaw outgrows the upper, resulting in an extended chin)

Neurological Manifestations

Affected individuals are often diagnosed with chronic fatigue syndrome, fibromyalgia, depression, hypochondriasis, and/or malingering prior to recognition of joint laxity and establishment of the correct EDS diagnosis

Brain "fog" (a sense of not being present; absence of focus or a lack of clarity)

Proprioception dysfunction (poor balance, klutzy)

Developmental coordination disorder

Somatosensory amplification

Severe headaches, including migraines, new daily persistent headache, cervicogenic headache, and neck-tongue syndrome

Headache attributed to spontaneous (idiopathic) cerebrospinal fluid leakage

Decreased deep tendon reflexes

Intracranial vascular abnormalities

Spinal stenosis (narrowing of spinal column)

Cerebral vascular accidents (strokes) in infancy (Vascular)

Delayed onset and/or resistance to local anesthesia

Slower-than-normal gait with shorter gait length (Hypermobility)
Peripheral neuropathy (weakness, numbness and pain from nerve damage, usually in the hands and feet)

Brachial plexus palsy (some or all of the arm muscles don’t work)

Sleep apnea

Lumbosacral plexopathy

Dural ectasia (widening or ballooning of the dural sac surrounding the spinal cord)

Ankles demonstrate excess plantar flexion at ground contact and decreased dorsiflexion during motion

Myalgias with cramps

Chronic, recurrent pain

Cerebrospinal fluid leak through the ear or nose (Classical)

Dolichocephaly (the head is disproportionally long and narrow)

Prominent supraorbital ridges (the ridge of bone above each eye)

Chiari malformation type I (the brain tonsils protrude down through the forum at the base of the brain)

Psychiatric Manifestations

Psychological dysfunction, psychosocial impairment and emotional problems are common

Specific manifestations may include affective disorder, low self-confidence, negative thinking, hopelessness, and desperation

Fatigue and pain exacerbate the psychological dysfunction

Psychological distress exacerbates pain

Fear of pain and/or joint instability may lead to avoidance behavior and exacerbate dysfunction and disability

Affected individuals may feel misunderstood, disbelieved, marginalized and alone

Resentment, distrust, and hostility may develop between the affected individual/family and the healthcare team (in both directions), adversely affecting the therapeutic relationship

Somatosensory amplification

High rates of anxiety and panic disorders, depression, anger and interpersonal concerns

Eye Manifestations

High myopia/nearsightedness (more than -6.0 diopters) and vitreous degeneration (16% of EDS eyes)

Detached retinas and ectopia (displaced) lenses
Photophobia (an abnormal sensitivity to or intolerance of light)
Tilted optic disc
Unilateral ptosis (dropping or falling of the upper or lower eyelid of one eye)
Slightly increased corneal curvature, keratoconus (cone shaped cornea)
Blepharochalasis (inflammation of the eyelids)
Xerophthalmia (failure to produce tears) is rare, but more likely than in the general population
Cataracts (cloudy lens)
Antimongoloid palpebral slant

Palpebral slant

Glaucoma (increase in intraocular pressure which leads to vision impairment)
Macular degeneration (macula atrophies, causing pigment changes and loss of central vision)
Angioid streaks (cracks in the Bruch’s membrane; broad, irregular, red to brown to grey lines which radiate from the area around the optic nerve head under the retinas)
Carotid-cavernous sinus fistulas (ruptured blood vessel that bleeds into the eye)
Posterior staphyloma (stretching/distortion of the back of the eye, causes increased nearsightedness)
Clinically insignificant minor lens opacities were found in 13% of EDS eyes
Easy eversion of eyelids (Menetrier sign)
Large pupils due to dysautonomia
Eye exams can cause vertigo, nausea and headache
Astigmatism
Early presbyopia (need reading glasses earlier)
Scleral fragility (Kyphoscoliosis)
Blue sclera (caused by visible uveal blood vessels through thinner sclera) (Dermatosparaxis
and
Spondylocheirodysplasia)

Micro cornea
Strabismus, eye turns, crossed eyes, wall-eyes, wandering eyes, deviating eye

Epicanthal folds (Classical)

Wide-spaced eyes

**Hematologic Manifestations**

Menometrorrhagia (prolonged or excessive uterine bleeding occurs irregularly and more frequently than normal)
Easy bruising, frequently without obvious trauma or injury, and frequently recurring in the same areas

Spontaneous epistaxis (nose bleed)

Bleeding from the gums, especially after dental extraction

Gynecologic Manifestations

Dyspareunia (painful intercourse) (77% of Classical & Hypermobility)

Sexual dysfunction

Pelvic instability (laxity and subluxation)

Pelvic prolapse (Classical & Hypermobility)

Vaginal dryness

Irregular menses

Meno/metrorrhagias (menstrual periods with abnormally heavy or prolonged bleeding and uterine bleeding at irregular intervals, particularly between expected menstrual periods)

Dysmenorrhea (painful periods) (92.5% of EDSers)

Endometriosis

Pelvic pooling

Pregnancy/Delivery Manifestations

Miscarriage/spontaneous abortion (57.2% of EDSers)

Bowel rupture, liver rupture, uterine rupture, postpartum hemorrhage (Vascular)

Extension of the episiotomy incision/perineal laceration (Classical & Hypermobility) – routine episiotomies are not recommended

Hematomas

Prolapse of the bladder or uterus related to delivery – avoid excessive traction on umbilical cord at time of delivery

Premature rupture of membranes (50% of Classical & Hypermobility vs. 20% of population)

Precipitous delivery (< 4 hours) (Classical & Hypermobility)

Cervical dilation may occur prematurely, resulting in premature birth (occurs in 50% of mothers with severe Classical type)

Pelvic floor dysfunction

Increased reflux during pregnancy

Anesthetic issues during labor & delivery (Classical & Hypermobility) – increased need for local anesthesia with EDS

With regional (spinal or epidural) anesthesia, hip and knee stress can cause dislocation

Slow-healing cesarean section incision (Classical & Hypermobility)

Peripartum arterial rupture or uterine rupture (Vascular -12% risk of maternal death)

Joint laxity and pain typically increase throughout gestation, especially in the third trimester (Hypermobility)

Anesthesia-induced hypotension

Meningeal fragility complicating in cerebrospinal fluid hypotension in case of epi/peridural anesthesia

Pelvic prolapse after episiotomy or vaginal tears

---Urinary stress incontinence

---Uterine prolapse
---Fecal incontinence

--- Suture dehiscence and minor hemorrhages after surgery

--- Cesarean section should be considered the first choice when vaginal delivery without episiotomy cannot be anticipated, in order to minimize the risk of pelvic prolapses

--- Ectopic pregnancy (5.1% of EDSers)

--- Infertility (44.1% of EDSers)
Neonatal/Childhood Manifestations

- Breech presentation
- Use of forceps or vacuum assistance on infant can cause lacerations and hematomas
- Prematurity (25.2% of EDS mothers)
- Joint laxity and severe muscle hypotonia at birth (Kyphoscoliosis)
- Hypotonia, floppy baby with articular hyperextensibility (Classical)
- Slightly preterm birth
- Congenital dislocations at shoulders and clavicles
- Early colic as a precursor to IBS
- Congenital hip dislocation, usually unilateral (3% of Vascular)
- Clubfoot (30% of Kyphoscoliosis and 12% of Vascular)
- Positional plagiocephaly
- Childhood failure to thrive due to IBS/low bowel motility
- Delayed or clumsy walking
- In-toeing due to joint flexibility

Urological/Abdominal Manifestations

- Giant bladder diverticula, which may cause urethral obstruction, is more common in male children with EDS
- Inguinal hernias
- Large umbilical hernias
- Visceroptosis [a prolapse or a sinking of the abdominal viscera (internal organs) below their natural position]
- Dysuria (painful urination)
- Urgency
- Bladder prolapse
- Nephrotic syndrome (the tiny blood vessels in the kidneys become leaky, allowing protein to pass out of the body in the urine)

Pain Manifestations

- Chronic pain, distinct from that associated with acute dislocations, is a serious complication that can be both physically and psychosocially disabling
- Chronic regional pain syndrome
- Pain is variable in age of onset (as early as adolescence or as late as the fifth or sixth decade), number of sites, duration, quality, severity, and response to therapy
- Severity is typically greater than expected based on physical and radiologic examinations
- Severity sometimes correlates with degree of joint instability and with sleep impairment
- Several recognizable pain syndromes are likely:
  - Muscular or myofascial pain, localized around or between joints, often described as aching, throbbing or stiff in quality, may be attributable to myofascial spasm, and palpable spasm with tender points is often demonstrable, especially in the paravertebral (beside the vertebral column) musculature.
Neuropathic pain, variably described as electric, burning, shooting, numb, tingling, or hot or cold discomfort, may occur in a radicular or peripheral nerve distribution or may appear to localize to an area surrounding one or more joints. Nerve conduction studies are usually non-diagnostic.

Osteoarthritic pain typically presents as aching pain in the joints, frequently associated with stiffness. It is often exacerbated by stasis and by resistance and/or highly repetitive activity.

Previous/Concurrent Diagnoses

- Chronic fatigue 82%
- Anxiety 73%
- Depression 69%
- Fibromyalgia 42%

Forms of Pain in Hypermobility Type

- **Nociceptive pain**
  - Soft-tissue injuries
  - Dislocations
  - Arthralgias
  - Back pain
  - Myalgias/myofascial pain

- **Neuropathic pain**
  - Compression neuropathy
  - Peripheral neuropathy

- **Dysfunctional pain**
  - Complex regional pain syndrome types I and II
  - Fibromyalgia
  - (Some) headache disorders
  - Functional abdominal pain
  - Dysmenorrhea (painful periods)
  - Vulvodynia/dyspareunia (vulval pain/painful intercourse)

Why More Women than Men are Diagnosed with Hypermobility Type

- 90% of HEDS patients who seek medical care are women
- Muscle pain perception differs in women and men
- Muscle size and ligament/tendon structure give men more joint stability
- Females tend to have more substantial joint laxity than males
- At puberty, sex hormones increase pain in women, muscle strength in men
Ten Musculoskeletal Characteristics Most Common in Hypermobility Syndrome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Incidence in 114 Subjects With HMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive ankle dorsiflexion and foot eversion(^a)</td>
<td>94%</td>
</tr>
<tr>
<td>Finger metacarpophalangeal joint extension past 90°(^a,b)</td>
<td>93%</td>
</tr>
<tr>
<td>Thumb abduction to the forearm(^a,b)</td>
<td>92%</td>
</tr>
<tr>
<td>Patellar hypermobility</td>
<td>89%</td>
</tr>
<tr>
<td>Excessive shoulder lateral rotation</td>
<td>84%</td>
</tr>
<tr>
<td>Excessive hip abduction</td>
<td>78%</td>
</tr>
<tr>
<td>Knee hyperextension past 10°(^a,b)</td>
<td>77%</td>
</tr>
<tr>
<td>Elbow hyperextension past 10°(^a,b)</td>
<td>75%</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>63%</td>
</tr>
<tr>
<td>First metatarsophalangeal joint extension past 90°</td>
<td>61%</td>
</tr>
</tbody>
</table>

Global measures appear to have greater sensitivity for identifying people with HMS than do isolated hyperextensometric measures. Symptoms do not appear to be directly correlated to the number of joints involved. That is, individuals with marginal scores on these tests may have more symptoms than do individuals with high scores.

Extra-articular Disorders Associated with Hypermobility Type

- Anxiety
- Carpal tunnel syndrome
- Chiari malformation type 1
- Chronic constipation
- Chronic fatigue syndrome
- Chronic regional pain syndrome
- Crohn’s disease
- Developmental coordination disorder
- Fecal incontinence
- Fibromyalgia
- Fixed dystonia
● Functional gastrointestinal disorder
● Headache attributed to spontaneous cerebrospinal fluid leakage
● Hiatus hernia
● Mitral valve prolapse
● New daily persistent headache
● Pelvic organ prolapse
● Postural tachycardia syndrome
● Psychological distress
● Rectal evacuatory dysfunction
● Somatosensory amplification
● Urinary stress incontinence

Morphologic and Orthopedic Features of Hypermobility Type

● Leptosomic built (androgy nous) or true Marfanoid habitus
● Dorsal hyperkyphosis
● Lumbar hyperlordosis
● Scoliosis of mild degree
● Fixed subluxation of the costochondral and/or steroclavicular joints
● Fixed dorsal subluxation of the distal radioulnar joint
● Fixed subluxation of the first carpometacarpal joint
● Cubitus valgus (increased carrying angle of the elbow)
● Femur anteversion (intoeing, kissing rotulae, and “W” position of the lower limbs at sitting)
● Patella alta or baja (higher or lower patella position than normal)
● Genu valgum (knocked knees)
● Flexible flatfoot
● Hallux valgus (bunion)
● High arched/narrow palate
● Facial asymmetry of mild degree (likely secondary deformational plagiocephaly)

Surgical and Anesthetic Issues in EDS Hypermobility Type

● Although surgery is not contraindicated in HEDS, the increased time requested for soft tissue repair and the related risk of possibly unsatisfactory results and muscle deconditioning due to postsurgical recovery entail to pay more attention in planning invasive interventions.
● The mild soft-tissue fragility and delayed wound healing may be counteracted by doubling the waiting time before suture removal.
● In case of local/minor surgery, consider the frequently reported resistance to intradermal lidocaine infiltrations and topical EMLA cream in HEDS; a double dose of anesthetic by intradermal injection as the first choice may be effective.
● Local anesthetic resistance could manifest also in case of epidural anesthesia.
● Intubation should be performed with care due to TMD and cervical spine instability and minor mucosal fragility; in adult patients with severe TMD dysfunction, limited mouth opening may request the use of pediatric devices.
Peridural anesthesia administration may request extra time due to premature spondylosis; meningeal fragility may associate with an increased risk of intracranial hypotension due to cerebrospinal fluid leakage.

In case of total anesthesia, the coexistence of cardiovascular dysautonomia may increase the risk of hemodynamic changes; prophylactic early fluid loading and phenylephrine infusion should be considered.

Although postsurgical hemorrhages are usually mild, their occurrence, especially in older subjects and toddlers as well as in case of concurrent chronic diseases, may expose the patient to unreasonable risks; prophylactic use of desmopressin (DDAVP) may be considered to reduce the chance of excessive bleeding.

Lifestyle Recommendations for EDS Hypermobility Type

- Promote regular, aerobic fitness
- Promote fitness support with strengthening, gentle stretching and proprioception exercises
- Promote postural and ergonomic hygiene, especially during sleep, at school, and at work
- Promote weight control (BMI < 25)
- Promote daily relaxation activities
- Promote lubrication during sexual intercourse (women)
- Promote early treatment of malocclusion
- Avoid high impact sports/activities
- Avoid low environmental temperatures
- Avoid prolonged sitting positions and prolonged recumbency
- Avoid sudden head-up postural change
- Avoid excessive weight lifting/carrying
- Avoid large meals, especially of refined carbohydrates
- Avoid hard foods intake and excessive jaw movements (ice, gum, etc.)
- Avoid bladder irritant foods (e.g., coffee and citrus products)
- Avoid nicotine and alcohol intake
- Dysautonomia-related fatigue may be partly managed by:
  - Generous daily water/liquid intake preferring isotonic solutions
  - High salt intake (unless you have arterial hypertension)
  - Daily supplementation of carnitine 250mg and/or coenzyme Q₁₀ 100mg

Ehlers-Danlos Syndrome Resources

Informational Websites
www.ednf.org (Ehlers-Danlos National Foundation)
www.dinet.org (Explains Dysautonomia/POTS)
www.tmsforacure.org (The Mastocytosis Society, Inc.)

Online Support Group
www.inspire.com/groups/ehlers-danlos-national-foundation/

Books


Hypermobility Type by Brad T. Tinkle, MD, PhD

A Multidisciplinary Approach to Managing Ehlers-Danlos (Type III) – Hypermobility Syndrome by Isobel Knight

A Guide to Living with Hypermobility Syndrome: Bending without Breaking by Isobel Knight

Hypermobility Syndrome: Diagnosis and Management for Physiotherapists by Rosemary Keer, MSc, MCSP, MACP and Rodney Grahame, MD, FRCP, FACP

Ehlers-Danlos Syndrome: Your Eyes and EDS by Diana Driscoll, O.D.

Hypermobility, Fibromyalgia and Chronic Pain by Alan Hakim, MB, FRCP, Rosemary Keer, MSc, MCSP, MACP and Rodney Grahame, MD, FRCP, FACP

A Zebra Like Me by Amy Maurer Jones (fictional-about a teenager with EDS)

Mayo Clinic Guide to Pain Relief by W. Michael Hooten, MD and Barbara Bruce, PhD

Medical Resource Guides (to print and give to your doctors)

http://www.ednf.org/resource-guides

EDNF Physicians Directory (to find an EDS-knowledgeable doctor near you)

http://www.ednf.org/ednf-physician-directory?shs_term_node_tid_depth=All&country=us&province=All