The Ehlers-Danlos Society

What are the Ehlers-Danlos syndromes?

The Ehlers-Danlos syndromes (EDS) are a group of connective tissue disorders that can be inherited and are varied, both in how they affect the body and in their genetic causes. They are generally characterized by joint hypermobility (joints that stretch further than normal), skin hyperextensibility (skin that can be stretched further than normal), and tissue fragility.

Connective tissue is the material in the body that binds together, supports, and separates different tissues and organs. Found between other tissues everywhere in the body, it provides strength and flexibility, and helps perform general functions as well as specialized services. Connective tissue disorders disrupt these most fundamental processes and structures of the body, so resulting problems can be widespread, in a wide range of severities, and affect areas that might seem to be otherwise unrelated.

Early diagnosis is crucial to positive patient health. Symptoms can be treated as they arise. Care is largely preventative, to support and manage EDS with the intent of keeping damage as minimal as possible. Specifics have to be tailored to those symptoms exhibited in the person with EDS. EDS is known to affect people of all ages, races, and genders.

For more information,
ehlers-danlos.com

EDS are currently classified into thirteen subtypes. A person's physical signs and symptoms will be matched up to the major and minor criteria to identify the subtype that is the most complete fit. There is substantial symptom overlap between EDS and other connective tissue disorders, so a definitive diagnosis for EDS when the gene mutation is known—all but hypermobile EDS—also calls for confirmation by testing to identify the responsible variant for the gene affected.

Please remember that an individual's experience with an EDS is their own, and may not necessarily be the same as another person's experience. Diagnostic criteria are meant solely to distinguish an EDS from other connective tissue disorders, and there are many more possible symptoms for each EDS than there are criteria.

Classical [*COL5A1, COL5A2*, rarely *COL1A1*]
Classical-like [*TNXB*]
Cardiac-valvular [*COL1A2*]
Vascular [*COL3A1*, rarely *COL1A1*]: possibility of shortened lifespan; arterial rupture is the most common cause of sudden death.
Hypermobile [no identified cause]
Arthrochalasia [*COL1A1, COL1A2*]
Dermatosparaxis [*ADAMTS2*]
Kyphoscoliotic [*PLOD1, FKBP14*]
Brittle cornea syndrome [*ZNF469, PRDM5*]
Spondylodysplastic [*B4GALT7, B3GALT6, SLC39A13*]
Musculocontractural [*CHST14, DSE*]
Myopathic [*COL12A1*]
Periodontal [*C1R, C1S*]

The Ehlers-Danlos Society

What are the hypermobility spectrum disorders?

Hypermobility spectrum disorders (HSD) are a group of conditions related to joint hypermobility (JH). HSD are intended to be diagnosed after other possible answers are excluded, such as any of the Ehlers-Danlos syndromes (EDS). HSD, just like hypermobile EDS, can have significant effects on our health. Whatever the problems that arise, whatever the diagnosis, it is important that these effects are managed appropriately and that each person is treated as an individual. HSD and hEDS can be equal in severity, but more importantly, both need similar management, validation, and care. HSD is known to affect people of all ages, races, and genders.

Joint hypermobility is a term to describe the capability of joints to move beyond normal limits. It can exist by itself or be a part of a more complex diagnosis. Those with joint hypermobility in a couple of joints (fewer than five) have localized joint hypermobility (LJH). Those of us with joint hypermobility in five or more joints are described as having generalized joint hypermobility (GJH). GJH is often something we're born with and possibly inherited, although acquired forms of GJH exist.

The essential difference between HSD and hEDS lies in the stricter criteria for hEDS compared to the HSD and reflects the more likely hereditary and/or systemic nature of hEDS compared to HSD. **Treatment is more important than labels.**

For more information,
ehlers-danlos.com

Generalized HSD: GJH plus one or more secondary musculoskeletal manifestations identified below.

Peripheral HSD: JH limited to hands and feet plus one or more secondary musculoskeletal manifestations.

Localized HSD: JH at single joints or group of joints plus one or more secondary musculoskeletal manifestations.

Historical HSD: historical)GJH plus one or more secondary musculoskeletal manifestations.

Secondary Musculoskeletal Manifestations

Trauma (macro- and microtrauma);

Chronic pain;

Disturbed proprioception;

Other musculoskeletal traits (flat feet, misaligned bones in the elbow and big toes, mild to moderate scoliosis, kyphosis of the upper spine and lordosis of the lower spine).

Associated Problems Not Based in the Musculoskeletal System

There can be many associated issues not directly related to the mechanics of jJH. These associations are very real; they seriously affect quality of life and they need to be managed as part of treatment. The strongest (but not only) associations noted so far are anxiety disorders, orthostatic tachycardia, a variety of functional gastrointestinal disorders, and pelvic and bladder dysfunction. These additional problems need to be evaluated and treated when an HSD is diagnosed.

PoTS UK
POSTURAL TACHYCARDIA SYNDROME

A GP's Guide to PoTS

www.potsuk.org
info@potsuk.org

What is PoTS?

PoTS stands for postural tachycardia syndrome
First characterised and defined in 1993

PREVALENCE estimated to be 0.2%

Abnormal response by the autonomic nervous system to upright posture. In some, mechanism is lack of vasoconstriction on standing causing pooling of blood in abdomen and limbs, reduced venous return to heart, compensatory tachycardia and altered cerebral circulation

More common in females age 15-50

DISABILITY - equivalent to disability in heart failure + COPD

ASSOCIATED WITH

- hypermobile Ehlers-Danlos Syndrome and hypermobility spectrum disorder
- chronic fatigue syndrome /ME
- autoimmune conditions
- growth/puberty in children

When to suspect PoTS

SUSPECT PoTS in

- medically unexplained symptoms
- CFS/ME
- hypermobile patients

SYMPTOMS
3 commonest symptoms are

- lightheadedness (presyncope)
- fatigue
- palpitations

Other symptoms include

- fainting
- nausea, bloating, abdominal pain
- cognitive dysfunction - 'brain fog'
- poor sleep
- exercise intolerance
- shakiness, sweating
- postural headaches and migraines

SIGNS *occur on standing/prolonged sitting*

- tachycardia
- acrocyanosis - red/purple puffy hands and feet (50% of patients)

How is PoTS diagnosed?

DIAGNOSTIC CRITERIA
Sustained increase in heart rate of 30 beats per minute (40bpm in teenagers) from lying to standing associated with symptoms of PoTS.

STAND TEST -rest supine and record HR and BP. Then stand in a safe place and record BP and HR every 2 minutes to 10 minutes.

INVESTIGATIONS -exclude anaemia, hyperthyroidism, postural hypotension, phaeochromocytoma

MISDIAGNOSIS
Mean time to diagnosis is 7 years
Meantime 50% of patients receive a psychiatric misdiagnosis e.g. anxiety, depression, hypochondriasis
Other misdiagnoses - CFS/ME

REFERRAL
To a specialist with an interest in PoTS-there is a list on the PoTS UK website www.potsuk.org/doctors_nhs

How to manage PoTS

AVOID TRIGGERS - heat, large meals, alcohol - drugs that lower BP

FLUIDS - at least 2 litres /day in adults
SALT - Adults:+6g/day (unless contraindicated)

EXERCISE - initially supine, graduated regimen, can take 2 months to improve symptoms

POSTURAL MANOUVRES to avoid fainting - avoid prolonged standing, elevate legs, tense buttocks + thighs, fold arms, tiptoe)

COMPRESSION - class 2, waist high tights

DRUGS - include β blockers, calcium channel blockers, ivabradine, midodrine, fludrocortisone, clonidine, SSRI, desmopressin, pyridostigmine, octreotide

CBT - to help adjust to chronic illness

IV FLUIDS - in an emergency only

Author: Dr. Lesley Kavi, Version 1, Review Date 1 March 2021

[redacted] Moving w no tears → Jeannie DuBios

Hookahs (shoes

EDS Hydration Options

Increase your fluid and salt intake by consuming at least **100 ounces water daily** and at least **6,000 mg (3 teaspoons) of added sodium (salt) (equal to 2,500 mg sodium)** to your diet since patients with Ehlers-Danlos typically are dehydrated and tend to have symptoms related to changes in their blood pressure and heart rate.

Liquid IV:
Good for all EDS/POTS patients. Not recommended for patients diagnosed with diabetes or a mast cell disorder. Mix with water.

Vitassium Salt Sticks
Mast cell disorder friendly. Keto/low carb diet and diabetic friendly.

Normalyte:
Good for all EDS/POTS patients. Not recommended for patients diagnosed with diabetes. There is a PURE version that would be recommend for any patient with a mast cell disorder. Mix with water.

HydroRx:
Good for all EDS/POTS patients. Not recommended for patients diagnosed with a mast cell disorder. Keto/low carb diet and diabetic friendly.
Mix with water.

Pedialyte AdvancedCare Plus Electrolyte Powder Packets/Solution:
Good for all EDS/POTS patients. Not recommended for patients diagnosed with diabetes or a mast cell disorder. Mix with water.

Gatorlytes:
Mast cell disorder friendly. Keto/low carb diet and diabetic friendly.
Mix with water.

* EDS = Ehlers Dantos Syndrome
* POTS = Postural Orthostatic Trachycardia Syndrome

EDS Resources

Websites

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

National Organization for Rare Disorders (NORD)
https://rarediseases.org/rare-diseases/ehlers-danlos-syndrome/

Dysautonomia International
Http://www.dysautonomiainternational.org/

The Dysautonomia Project
https://thedysautonomiaproject.org/

The Mastocytosis Society
https://tmsforacure.org/

Books

Understanding Hypermobile Ehlers-Danlos Syndrome & Hypermobility Spectrum Disorders by Claire Smith

Living Life to the Fullest with Ehlers-Danlos Syndrome: Guide to Living a Better Quality of Life While Having EDS by Kevin Muldowney

Joint Hypermobility Handbook- A Guide for the Issues & Management of Ehlers-Danlos Syndrome Hypermobility Type and the Hypermobility Syndrome by Brad Tinkle

A Guide to Living with Ehlers-Danlos Syndrome (Hypermobility Type): Bending without Breaking (2nd edition) by Isobel Knight and Alan Hakim

The Dysautonomia Project: Understanding Autonomic Nervous System Disorders for Physicians and Patients by Kelly Freeman, David S. Goldstein, et al.

Never Bet Against Occam: Mast Cell Activation Disease and the Modern Epidemics of Chronic Illness and Medical Complexity by Lawrence B. Afrin M.D., Kendra Neilsen Myles, et al.

Kinesiology Taping The Essential Step-By-Step Guide: Taping for Sports, Fitness and Daily Life - 160 Conditions and Ailments by John Langendoen and Karin Sertel

Groups

Cincy Zebras (meets at TriHealth Wellness Pavilion Monthly)
Https://www.facebook.com/groups/cincyzebras/
cincyzebras@gmail.com

The Mighty

https://themighty.com/topic/ehlers-danlos-syndrome/

For more information, please call 513 853 1300 for the EDS Navigator.

hEDS Diagnostic checklist: https://www.ehlers-danlos.com/heds-diagnostic-checklist/

<table>
<tr><th colspan="4">Criteria: All 3 must be met</th></tr>
<tr><td colspan="2">CRITERION 1: GJH
Must meet Beighton Score for age</td><td colspan="2">CRITERION 2: At least 2 features must be present</td></tr>
<tr><td>Age</td><td>Beighton Score (see Table 3)</td><td rowspan="4">Feature A: Systemic manifestations of CTD (need ≥5)
1. Unusually soft/velvety skin
2. Mild skin hyperextensibility
3. Unexplained striae distensae/rubrae
4. Bilateral piezogenic papules of heel
5. Recurrent/multiple abdominal hernia
6. Atrophic scaring in ≥2 sites
7. Pelvic floor, rectal, and/or uterine prolapse in children, men or nulliparous women
8. Dental crowding and high or narrow palate
9. Arachnodactyly
10. Arm span-to-height ≥1.05
11. Mitral valve prolapse
12. Aortic root dilatation with Z-score > +2</td><td rowspan="4">Feature B: Family history (1 or more first degree relatives must meet criteria)

Feature C: MSK Complications (need ≥1)
1. MSK pain in ≥2 limbs, recurring daily for ≥3 months
2. Chronic widespread pain for ≥3 months
3. Recurrent joint dislocations or frank joint instability, in the absence of trauma (a or b)
a. ≥3 atraumatic dislocations in same joint or ≥2 more atraumatic dislocations in two difference joints occurring at different times
b. Medical confirmation of joint instability at two or more sites not related to trauma</td></tr>
<tr><td>Prepubescent or adolescent</td><td>≥6</td></tr>
<tr><td>Pubescent up until age 50</td><td>≥5</td></tr>
<tr><td>Over age 50

Patients with AJLs</td><td>≥4

BS 1 point under age requirements AND a positive 5PQ (see Table 4)</td></tr>
<tr><td colspan="4">CRITERION 3: All 3 prerequisites must be met</td></tr>
<tr><td colspan="4">1. Absence of unusual skin fragility.
2. Exclusion of other heritable and acquired connective tissue disorders. In patients with an acquired connective tissue disorder, additional diagnosis of hEDS requires meeting both Features A and B of Criterion 2. Feature C of Criterion 2 cannot be counted in this situation.
3. Exclusion of alternative diagnoses that may also include joint hypermobility by means of hypotonia and/or connective tissue laxity.</td></tr>
</table>

Healthcare professional directory: https://www.ehlers-danlos.com/medical-professionals-directory/

hEDS/HSD RESOURCES

This is a collection of resources that could be utilized by a provider as tools or references for their practice or to compile a resource list for patients. This is not a comprehensive or medically vetted list.
For word doc, please email Gretchen MacCarrick, goswald1@jhmi.edu, *(edited 9/3/21 for NSGC AEC)*

Welcome to the world of EDS: tips and tricks for the newly diagnosed:
https://www.youtube.com/watch?v=WqTiSHTk39A

Resources for Patients and Families (comprehensive):
https://www.mountainstatesgenetics.org/projects/eds-algorithm/

Therapies
Find a Mindfulness Based Stress Reduction program: https://umassmed.edu/cfm/mindfulness-based-programs/mbsr-courses/find-an-mbsr-program/
Find a Cognitive Behavioral therapist directory:
https://services.abct.org/i4a/memberDirectory/index.cfm?directory_id=3&pageID=3282

POTS:
The Levine Protocol: https://chronicallysalty.com/2019/03/06/the-levine-protocol-what-it-is-and-how-it-helps-pots/
https://chronicallyawesome.org.uk/levine-protocol/

CHOP Modified Dallas POTS exercise protocol: on websites above or
https://chronicallysalty.files.wordpress.com/2018/05/chop_modified_dallas_pots_exercise_program.pdf

Dysautonomia International - Virtual Wellness Class: Supine Exercise for Beginners
https://vimeo.com/437867091
Dysautonomia International: http://www.dysautonomiainternational.org/
Dysautonomia International POTS http://www.dysautonomiainternational.org/page.php?ID=30

Mast Cell Disease:
The Mast cell disease society: https://tmsforacure.org/symptoms/symptoms-and-triggers-of-mast-cell-activation/

GI:
https://practicalgastro.com/2016/04/12/hypermobility-syndrome-and-gastric-emptying-disorders/
International Foundation for GI disorders: https://iffgd.org/

Headaches:
National headache foundation https://headaches.org/resources/#headache-tools

Chronic pain
Video of exercises: https://www.youtube.com/watch?v=ule37PdEIQk
Webinar: EDS Awareness webinars: https://www.chronicpainpartners.com/webinars/
Blog/resources: https://lifehypermobile.com/pain-management/pain-management-resources/
Arthritis learning modules: https://arthritis.ca/support-education/online-learning

Support groups:

EDS Society: https://www.ehlers-danlos.com/about-us/
-International and local resources: https://www.ehlers-danlos.com/affiliates-support-groups-and-charities/
EDS Awareness: https://www.chronicpainpartners.com/
Inspire hEDS group: https://www.inspire.com/groups/eds-and-hsd/
Hypermobility Syndrome Association: https://www.hypermobility.org/online-support-groups
EDS wellness: https://edswellness.org/

For providers:

EDS echo program: https://www.ehlers-danlos.com/echo/
- EDS ECHO® a program for healthcare professionals across all disciplines who want to improve their ability to care for people with EDS, HSD and associated symptoms and conditions.
The heart of the ECHO model™ is its hub-and-spoke knowledge-sharing networks, led by expert specialist teams. The ECHO model is not "telemedicine" where specialists assume the care of the patient; it is a guided model aimed at practice improvement, in which providers retain responsibility for patients, and gain increasing independence as skills, confidence, and self-efficacy grow.

UpToDate: https://www.uptodate.com/contents/overview-of-the-management-of-ehlers-danlos-syndromes

Ehlers-Danlos Syndrome (EDS) Algorithm and Resources for Primary Care
https://www.mountainstatesgenetics.org/projects/eds-algorithm/
-Mountain States Genetics resource with excellent patient care guides as well

Functional GI disorders and HSD:

https://qmro.qmul.ac.uk/xmlui/bitstream/handle/123456789/8301/A%20Fikree_PhD.pdf;sequence=1

Slidesets:

Pain relief/medication use: slideset of Dr. Chopra https://www.ehlers-danlos.com/2013-annual-conference-files/Chopra_Chronic_pain_and_EDS_Final_1slideS.pdf

"Hypermobility Meeting in a box": https://www.hypermobility.org/kent-model-resources

PT slide set/case example:

https://www.orthopt.org/uploads/content_files/files/A%20Zebra%20Among%20US.pdf
https://www.ehlers-danlos.com/2012-annual-conference-files/Riddle_hypermobility_presentation_v2_final.pdf
https://www.ashfordstpeters.info/images/leaflets/PY11.pdf

OT

https://www.cddft.nhs.uk/media/659664/hypermobility_ot%20info%20pack.pdf

Links to Joint Protection Information:

Joint Protection for your Hands: https://arthritis.ca/getmedia/4b9d8ef1-64c6-412a-93a7-6a6183910b7b/Joint-Protection-for-Your-Hands_updated-June-2020.pdf

Joint Protection for Hips and knees: https://arthritis.ca/getmedia/b916063c-370c-4627-881d-0bbba470c5ea/2019-Joint-Protection-for-Hips-and-Knees.pdf

Links to Braces/aids:

Ring splints:

Https://www.amazon.com/Oval-8-Finger-Splint-Graduate-Set/dp/B00GK8XC6U?th=1

Https://www.silverringssplint.com/problems-addressed/eds/

Kinesiology tape

https://www.youtube.com/watch?v=v0kX4MwdCvs)

https://theratape.com/module/landingpages/landingpage?id_landingpage=6&lp_rewrite=types-of-kinesiology-tape

Flexible soft braces (ankle, wrist)

https://jboccupationaltherapy.co.uk/splinting-types/

http://store.kinemedics.com/orthopaedic-bracing.html

http://orthomedix.com/custom-braces/

https://www.wellwise.ca/products/category/braces-and-supports/wrist-brace-and-supports

Compression support:

http://store.kinemedics.com/orthopaedic-bracing/compression-garments.html?mode=list

Inflatable neck collar:

https://www.amazon.ca/Banglijian-Cervical-Inflatable-Effective-Adjustable/dp/B0859J738Z

Forearm crutches:

https://www.sidestix.com/

https://www.smartcrutch.com/

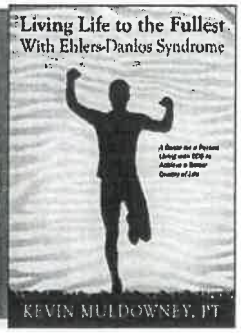
Footwear Brochures: https://arthritis.ca/getmedia/c1a81cf2-5003-4a44-a9c8-d1fce119fc49/13-Footwear.pdf

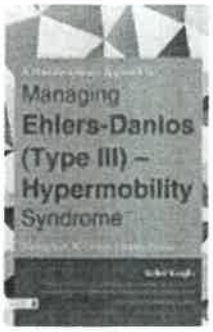
Focused Breathing Exercise: https://arthritis.ca/getmedia/59f1fcc6-60c0-432a-bfd3-79b10ecd84c6/06-Focused-Breathing-Exercise.pdf

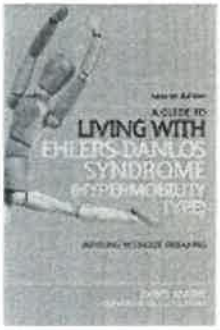
Cold Therapy: https://arthritis.ca/getmedia/6b88faca-5313-468f-b227-c5f5cf662c3d/03-Cold-Therapy.pdf

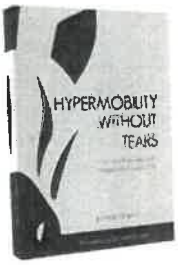
Heat Therapy: https://arthritis.ca/getmedia/4c02c37f-a239-414b-bd7d-54a81a22c462/04-Heat-Therapy.pdf

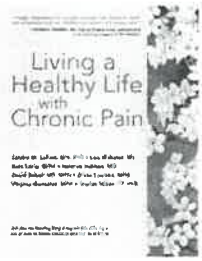
BOOKS:

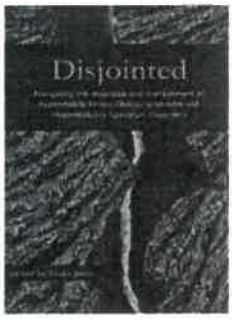












1. Dr. Bradley Tinkle: "Joint Hypermobility Handbook- A Guide for the Issues & Management of Ehlers-Danlos Syndrome Hypermobility Type and the Hypermobility Syndrome'; amazon.com

2. Rosemary J Keer and Rodney Grahame (resource for PTs): "Hypermobility Syndrome: Diagnosis and Management for Physiotherapists"; amazon.com

3.Claire Davies (resource for myofascial trigger point release at home to address muscle spasms and myofascial pain): "The Trigger Point Therapy Workbook;" amazon. Com (https://www.painscience.com/tutorials/trigger-points.php)

4. In general, mindfulness-based stress reduction can aid in coping with chronic pain. A good resource is Dr. Jon Kabat-Zinn's books called "Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness" and "Wherever You Go, There You Are."

5. JWG Jacobs, LJM Cornelissens, MC Veenhuizen, BCJ Hamel "Ehlers-Danlos Syndrome: A MultiDisciplinary Approach". 370 page e-book (or can order hard copy). http://ebooks.iospress.nl/ISBN/978-1-61499-878-5

6.Kevin Muldowney, PT "Living Life to the Fullest with Ehlers-Danlos syndrome". A guide for a person living with EDS to achieve a Better quality of life. Amazon.com

7. Diana Jovin. Disjointed | Navigating the Diagnosis and Management of hypermobile Ehlers-Danlos Syndrome and Hypermobility Spectrum Disorders. Amazon.com

8. Isobel Knight, " A Guide to Living with Ehlers-Danlos Syndrome (Hypermobility Type): Bending without Breaking (2nd edition)." Amazon.com

9. Various EDS journals for tracking pain, mood, diet, symptoms, treatment, etc. Amazon.com

Podcasts:

Podcasts: Hypermobility happy hour: https://www.chronicpainpartners.com/hypermobility-happy-hour-podcast-with-dr-linda-bluestein/

Bendy Bodies Podcast | Hypermobility https://www.hypermobilitymd.com › podcast

Live Yes! With Arthritis: https://www.arthritis.org/liveyes/podcast

Finding Your Range Podcast: Hypermobility and Chronic Pain uncovered: https://jeanniedibon.podbean.com/

Listing of EDS podcasts: https://player.fm/podcasts/Ehlers-Danlos

Literature (patients or providers)

GeneReviews: http://www.ncbi.nlm.nih.gov/books/NBK1279/

In March, 2017, the American Journal of Medical Genetics Part C: Seminars in Medical Genetics was dedicated to Ehlers Danlos syndrome. These articles are available at https://www.ehlers-danlos.com/2017-eds-international-classification/

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2. The 2017 international classification of the Ehlers–Danlos syndromes (pages 8–26)
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Ghali, Cecilia Giunta, Rodney Grahame, Alan Hakim, Xavier Jeunemaitre, Diana Johnson, Birgit Juul-Kristensen, Ines Kapferer-Seebacher, Hanadi Kazkaz, Tomoki Kosho, Mark E. Lavallee, Howard Levy, Roberto Mendoza-Londono, Melanie Pepin, F. Michael Pope, Eyal Reinstein, Leema Robert, Marianne Rohrbach, Lynn Sanders, Glenda J. Sobey, Tim Van Damme, Anthony Vandersteen, Caroline van Mourik, Nicol Voermans, Nigel Wheeldon, Johannes Zschocke and Brad Tinkle

3. Ehlers–Danlos syndrome, classical type (pages 27–39)
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4. Diagnosis, natural history, and management in vascular Ehlers–Danlos syndrome (pages 40–47)
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5. Hypermobile Ehlers–Danlos syndrome (a.k.a. Ehlers–Danlos syndrome Type III and Ehlers–Danlos syndrome hypermobility type): Clinical description and natural history (pages 48–69)
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6.The Ehlers–Danlos syndromes, rare types (pages 70–115)
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Measurement properties of clinical assessment methods for classifying generalized joint hypermobility—A systematic review (pages 116–147)
Birgit Juul-Kristensen, Karoline Schmedling, Lies Rombaut, Hans Lund and Raoul H. H. Engelbert

7. A framework for the classification of joint hypermobility and related conditions (pages 148–157)
Marco Castori, Brad Tinkle, Howard Levy, Rodney Grahame, Fransiska Malfait and Alan Hakim

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Treatments

Orthostatic Intolerance–Increase fluids and salt intake by consuming at least 100oz (about 3 liters) of water daily and at least 4000 mg (2 tsp) of added salt to your diet. People with EDS are typically dehydrated and tend to have symptoms related to changes in their blood pressure and heart rate. An easy way to supplement your salt intake is to start using an over the counter product water additive such as liquid IV or Pedialyte Advanced Care Plus power packs (available in stores or online).

Medications are sometimes used but should be additions to the increased fluid intake and exercise, not substitutions. Intravenous fluids are sometimes given on an as needed basis but should be limited and used as a last resort. Medications to improve fluid reabsorption, such as fludrocortisone have been used in patients with autonomic dysfunction. Diuretics (water pills), including spironolactone, should be avoided where possible. Midodrine helps redirect blood flow away from the extremities toward the brain. It can cause high blood pressure when lying down, so is typically used during the day, but not at night.

Compression stockings–(available at a pharmacy, in stores or online)- are specially made, snug-fitting, stretchy socks that gently squeeze your legs. They help improve the blood flow in your legs, support veins and decrease swelling. They can also help reduce orthostatic hypotension which can cause lightheadedness or unsteadiness when you stand.

Therapy–Physical therapists help to identify and treat issues related to EDS with core strengthening and exercises to improve balance and stability. Many patients have had site-specific physical therapy (e.g. knee or back) and may feel that physical therapy "does not work for them. "The physical therapy for a hypermobile patient is different, often looked at as an "inside out" strategy because it starts from the center of the body. Therapists who are not trained in care of an EDS patient or its treatment strategy may produce less successful results.

Increased physical activity–At least 30 minutes of exercise, helps move oxygen through the blood and raises your rate of breathing is recommended 5 days a week. This can be swimming, water aerobics and recumbent bikes, which is usually the best tolerated. Avoid contact sports and other activities, like running, that could hurt your joints.

Aquatic therapy–is typically used as an initial strategy for those who are unable to tolerate upright exercise due to pain or autonomic symptoms. It has the advantage of floating in the water to reduce pain on the joints.

Pain Medications–Pain management is similar to that of fibromyalgia, since they are closely related. Patients are often started on ibuprofen, acetaminophen or naproxen. After that, medications such as Lyrica, Neurontin, Elavil, Cymbalta or Savella might be used. Round-the-clock usage of narcotics or muscle relaxers is not recommended as these decrease muscle tone, which defeats the purpose of physical therapy. A referral to a pain management clinic may be given when simple solutions are not working.

Mast Cell Activation and GI Issues–Zyrtec and Pepcid, both available over-the-counter, can help with relief of symptoms. Allergists may be involved if additional medications are needed.

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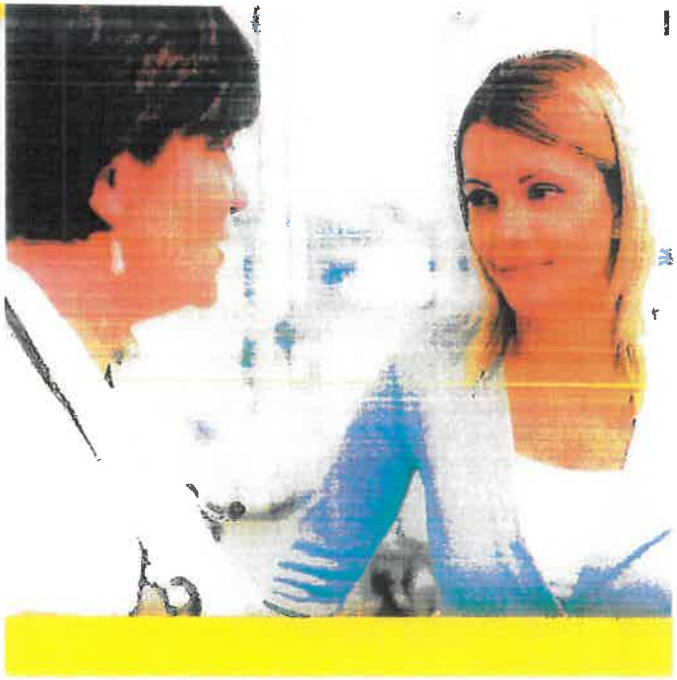

Ehlers-Danlos Syndrome and Hypermobility Spectrum Disorders

TriHealth

What is Ehlers-Danlos Syndrome?

Ehlers Danlos Syndrome (EDS) is the name for a group of diseases that cause the bodies connective tissues to be too loose, stretchy or fragile. Connective tissues hold our cells together and make up and support the skin, bones, blood vessels and other organs. With EDS, collagens which are a protein in the body that helps to build connective tissue, does not form correctly.

Most forms of EDS are caused by a genetic mutation in the collagen genes. The genetic mutation can be inherited, meaning if a family member such as a parent has it, there is a 50-50 chance of passing that genetic mutation onto their child. There are genetic tests available for some but not all types of EDS. The most common type of EDS which is the Hypermobile EDS or EDS-HT, does not have a genetic defect that has been visible in enough detail to allow accurate genetic testing. It is believed that it may have multiple genetic causes, that makes the process of identifying the gene difficult. With EDS, girls and boys are equally affected but in adolescence it is often observed that the boys get better and the girls get worse. Due to this in adulthood, women tend to be more severely affected then men.

Diagnosis

Due to being unable to diagnose EDS-HT with genetic testing, diagnosis is based on a pattern of symptoms, an assessment of joint flexibility (the Beighton Scale), and evaluation of other changes in the skin, other tissues, and family history.

Prevalence and Hypermobility as a finding: EDS-HT is far more common than initial estimates. We now believe that it may occur as much as 1 in 400 persons. Joint hypermobility (being overly flexible) that presents without symptoms is even more common at about 1 in 10, depending on the population. So, at what point does hypermobility become EDS-HT? It is called EDS-HT when the symptoms disrupt daily living.

Symptoms of EDS-HT:

Chronic pain—This pain is usually from a combination of muscle, tendon or ligament strain. The pain can be felt at the place of injury, but it may also be felt where the ligament or tendon attaches to the bone. It is easiest to recognize this process in children who have "growing pains". For most children, looseness of the foot muscle causes it to flatten. This causes the knee to move toward the middle. The muscles of the thigh must then pull the knee outward, causing a pain in the outer thigh muscles typically felt at night after a busy day of walking or running. In order to pull, the abductor muscles must block the adductor muscles (which pull the knee inward), done through a nerve reflex. Because of repeated blocking, we typically see the adductor muscles become weak. This mixed pattern of tension and weakness allows the process to continue. As patients age and grow, this pattern becomes more widespread, often causing pain in the hips, back, shoulders, and neck. While dislocations and patterns of injuries can be easily seen, what is not seen is that people with EDS have decreased body awareness and have problems realizing the body's position in relation to other objects. The brain uses the many signals of muscle tension and length to be aware of body position. Since those signals don't work correctly, the brain must "guess" the body's position or use other senses to adjust, which causes people with EDS-HT to have balance issues and be clumsy.

Symptoms:

Stretchy skin—the skin stretches more than normal if pulled. The medical term for this is hyperextensibility.

Thin skin/Easy bruising of the skin—skin is easily scratched and cut. Cuts may take longer to heal and may also leave abnormal looking scars.

Joints are too loose and more flexible than normal—The medical term for this is Hypermobility. Loose joints can lead to problems such as dislocations (when joints pop out of place) or pain.

Orthostatic Intolerance—Dizziness, Lightheadedness, or Blacking-Out when standing up. Symptoms are those typically seen in the fight-or-flight response, which is also a fear reaction: Panic, anxiety, racing heartbeat, elevated blood pressure, rapid breathing, pale skin and dry mouth. Additionally, the fight-or-flight response shuts down sleep, making a person awake and vigilant. It may slow down digestion, leading to nausea, inability to eat and abdominal pain.

Increased Histamine Response—Some patients will have more episodes of flushing, hives, itching and diarrhea in response to foods or environmental allergies. These responses are caused by histamine, which is released by mast cells. Mast cells are part of the immune system that play a role in inflammation, help fight infections, and are involved in wound healing and tissue repair. Histamine causes blood vessels to dilate and become leaky. Some patients have overactive responses due to "mast cell activation syndrome," which is a condition in which the mast cells respond to many different triggers. Treatment includes treating allergy symptoms and avoiding triggers. Some foods may trigger symptoms but be aware that medications, especially narcotics, can trigger histamine release.

Migraines/Chronic Headaches—EDS patients commonly suffer a variety of headache types. These include headaches due to migraines (long-lasting headaches, usually felt as a pulsing pain on one side of the head), muscle tightness, high blood pressure and other physical conditions. Migraines are more common in women than men. EDS may be considered a risk factor for migraines. Many migraine therapies exist and should be discussed with your EDS provider.

Gum Disease—Some types of EDS increase the risk of periodontitis, a severe gum infection that can lead to tooth loss and other serious health problems. Good oral hygiene reduces the risk of periodontal disease. Individuals with periodontal disease should be treated by a specialist in periodontology who will be able to provide professional cleaning of the teeth and gums and when needed, surgery to improve the gum health.

Temporomandibular joint disorder (TMJ)—can cause pain and problems of the jaw joint and the muscles that control jaw movement. EDS patients are thought to be at a higher risk for this due to the hypermobility of the Temporomandibular Joint.

Irritable Bowel Syndrome/Chronic Constipation and/or Slower gastric emptying—These are problems such as changes in the speed of the digestive system. Patients with EDS show gastrointestinal symptoms related to the gut and are often diagnosed with indigestion and irritable bowel syndrome.

Hormones—Hormones seem to play a role in the acceleration of symptoms in women. This is commonly seen with puberty and pregnancy. More specifically during pregnancy, the hormone relaxin is released and its job is to break down connective tissue. Because of this, many women report feeling worse with each pregnancy.

OUR STRENGTH BEGINS WITH HOPE

GET IN TOUCH

For more information on The Society's work, to get involved, or to donate, please visit:

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WHAT WE DO

COLLABORATIVE RESEARCH
Bringing together medical professionals from all over the world to work on groundbreaking management and care.

MEDICAL & SCIENTIFIC SYMPOSIUMS
To examine the latest research and update the diagnostic criteria and guidelines for management and care.

COMMUNITY
Bringing together and uniting our community, providing annual conferences globally to distribute information and create opportunities to interact.

MEDICAL LITERATURE
Producing reliable up-to-date medical literature though our esteemed medical and scientific board and International Consortium on EDS and Related Disorders.

RESOURCES, SUPPORT & EDUCATION
Guiding both patients and medical professionals to the most up to date information, resources, support and education.

SUPPORT GROUPS & CHARITIES
Uniting support groups and charities from around the world, providing resources and information where needed.

AFFILIATE PROJECTS
Working with our Affiliates on local issues and projects that affect our communities around the globe. One person fighting is a start, but many together build an army.

The Ehlers Danlos Society

WHO WE ARE & WHAT WE DO.

THE EHLERS-DANLOS SOCIETY

The Ehlers Danlos Society

WHO WE ARE

The Ehlers-Danlos Society is a global community of patients, caregivers, healthcare professionals and supporters dedicated to saving and improving the lives of those affected by the Ehlers-Danlos syndromes and related disorders.

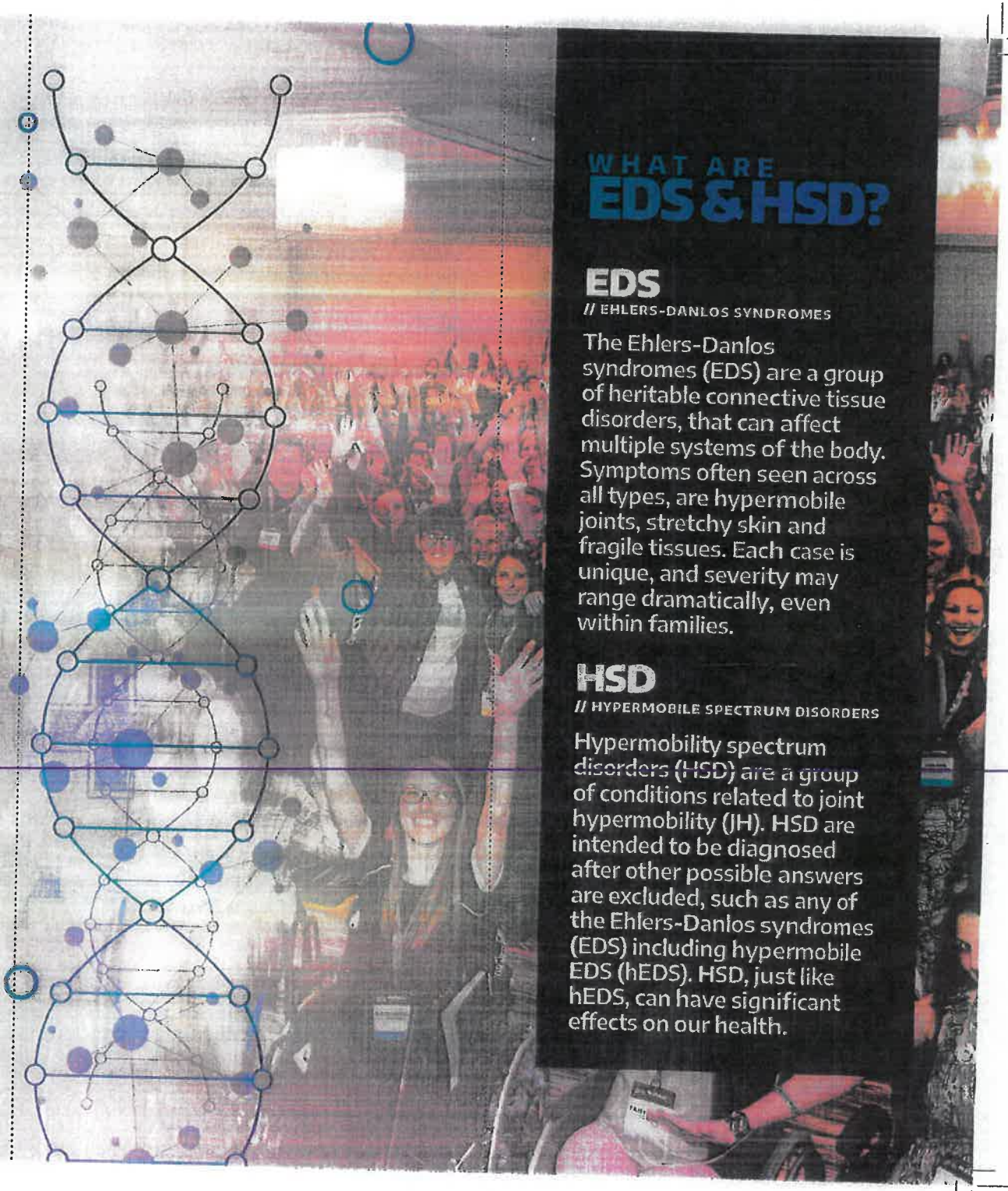
We are a non-profit organization, established in 1985 as the Ehlers-Danlos National Foundation by Nancy Hanna Rogowski (1957–1995).

Our Mission

We support collaborative research and education initiatives, awareness campaigns, advocacy, community-building, and care for the Ehlers-Danlos Syndromes (EDS) and Hypermobility Spectrum Disorders (HSD) population.

Our goals are world-wide awareness and a better quality of life for all who suffer from these conditions. Research is at the center of what we do, so that one day we will have a cure.

Our Strength Begins With Hope.



WHAT ARE EDS & HSD?

EDS
// EHLERS-DANLOS SYNDROMES

The Ehlers-Danlos syndromes (EDS) are a group of heritable connective tissue disorders, that can affect multiple systems of the body. Symptoms often seen across all types, are hypermobile joints, stretchy skin and fragile tissues. Each case is unique, and severity may range dramatically, even within families.

HSD
// HYPERMOBILE SPECTRUM DISORDERS

Hypermobility spectrum disorders (HSD) are a group of conditions related to joint hypermobility (JH). HSD are intended to be diagnosed after other possible answers are excluded, such as any of the Ehlers-Danlos syndromes (EDS) including hypermobile EDS (hEDS). HSD, just like hEDS, can have significant effects on our health.

JOIN EDS ECHO®

Project ECHO®

EDS ECHO
The Ehlers-Danlos Society

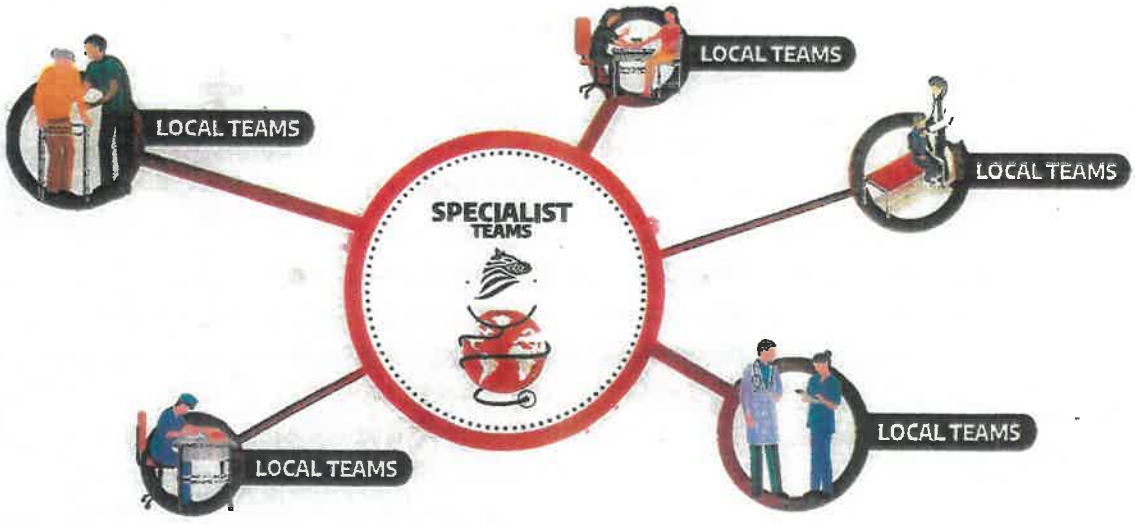
The Ehlers-Danlos Society partnering with Project ECHO®

Enhancing care for people with all types of Ehlers-Danlos syndrome (EDS) and hypermobility spectrum disorder (HSD) through case-based discussions, sharing knowledge and expert updates

EDS ECHO offers a variety of programs for health care professionals across all disciplines and community leaders and educators who want to improve their ability to care for and support people with EDS, HSD and associated symptoms and conditions.

Project ECHO addresses population health in a scalable way - moving knowledge instead of patients via telementoring and collaborative care.

The heart of the ECHO model™ is its hub-and-spoke knowledge-sharing networks, led by expert specialist teams. The ECHO model is not "telemedicine" where specialists assume the care of the patient; it is a guided model aimed at practice improvement, in which providers retain responsibility for patients, and gain increasing independence as skills, confidence, and self-efficacy grow.



→ To find out more, please turn over

The **Ehlers-Danlos** Society

www.ehlers-danlos.com

The Ehlers-Danlos Society is a global charity dedicated to improving the lives of those with all types of Ehlers-Danlos syndrome (EDS), hypermobility spectrum disorders (HSD), and associated symptoms and conditions.

EDS ECHO® An Evolution in Medical Education and Care Delivery

- EDS ECHO has programs running from North America, Europe, and Australasia.
- Over time, our aim is to open hubs and networks all over the world.
- Clinical experts run programs in Childhood, Adolescent, and Adult Medicine that cover all aspects of EDS and HSD.
- Participants share their cases and questions in the sessions and are guided to further educational materials and support.
- CME/CPD educational credits are available on selected programs and on courses.
- After taking part in a healthcare professional program, participants are invited to join us at any future EDS ECHO sessions and continue to take advantage of and support our ever-growing network of knowledgeable clinicians. We also help local and regional groups to start a program for the care of their patients, expanding the EDS ECHO network, bringing care closer to home.

- We support collaborative research and education initiatives, awareness campaigns, advocacy, community-building, and care for the EDS and HSD population.
- One of our greatest assets is our International Consortium, a group of independent expert clinicians, scientists, and patients from across many specialties. Our medical professional members run the EDS ECHO program.
- We will also help interested groups to start a program for the care of their patients, expanding the EDS ECHO network, and bringing care closer to home.

Join Us!

Go to our webpage:

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Here you will find:

- Details of the upcoming programs
- How to join

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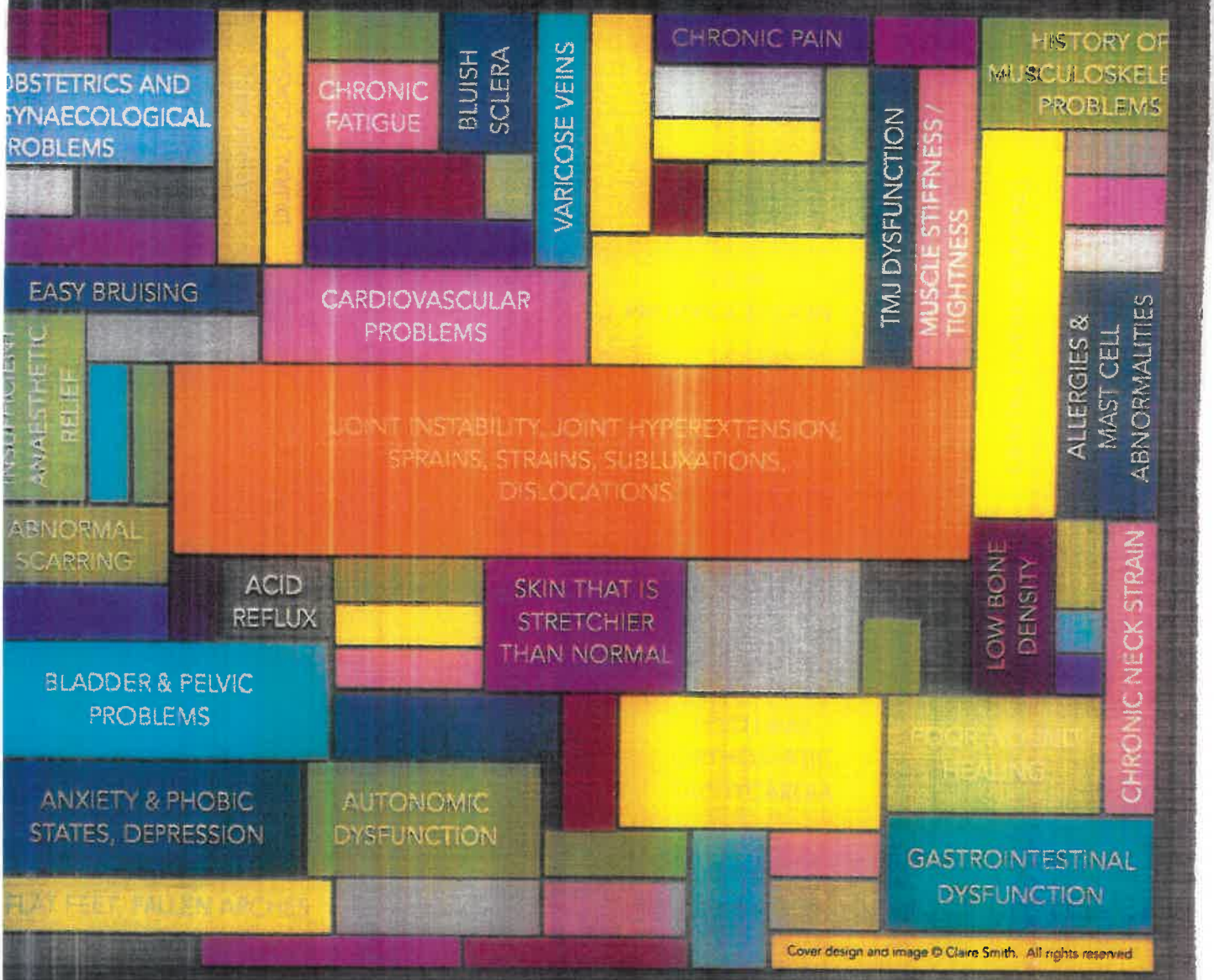
Understanding Hypermobile Ehlers-Danlos Syndrome and Hypermobility Spectrum Disorder

(previously known as Ehlers-Danlos syndrome hypermobility type & joint hypermobility syndrome, respectively).

by Claire Smith



Principles of Therapy for Ehlers Danlos Hypermobility Type

Derek Neilson, MD
Cincinnati Children's Hospital Medical Center
Connective Tissue Clinic

Dear Doctors and Patients,

There are many different explanations for chronic pain and other chronic conditions. EDS-HT represents a physical disorder in which the pathogenesis of chronic ailments can be understood in a new or different way. The ability to explain the origin of symptoms helps pave the way to address the underlying problems.

Our clinic at CCHMC evaluates approximately 900 patients per year for disorders of Connective Tissue. This gives us excellent opportunity for pattern recognition, but our clinic has become overwhelmed with new patient requests that we can no longer accommodate. The intent of our learning conference is to help educate patients and physicians which will hopefully bring about better interaction between patient and physician. This short paper summarizes what the learning conference and will describe EDS-HT and its therapies that have been successful, pointing out along the way how it is different than typical. It has been written to bridge medical terminology and layman's speech.

Genetics: EDS-HT is a disorder of connective tissue, but the genetic defect has not been identified in sufficient detail to allow genetic testing. Indeed, there may be multiple genetic causes, which makes the process of gene-finding difficult. As such, the diagnosis is purely clinical and depends on a joint scoring system (the Beighton Scale), mild skin changes (striae, mild elasticity, weakened scars), and family history. While the genetic cause is unknown, there is clearly dominant inheritance in the majority of families we evaluate, meaning that the disorder passes from parent to child.

Prevalence and Hypermobility as a finding: EDS-HT is far more common than initial estimates. We now believe that it could occur as much as 1 in 200 persons. Hypermobility as an asymptomatic state is even more common at about 1 in 10, depending on the population. This can be confusing as it begs the question, at what point does hypermobility become EDS-HT? Our answer remains practical—we call it EDS-HT when the associated symptoms disrupt daily living. This makes the definition less satisfying from a genetic perspective, as we like "clean" answers. However, the practical application is that a patient with EDS-HT can approach their symptoms from a different therapeutic perspective, which we find more successful.

Associated Symptoms: The associated problems with EDS-HT reads like a loose aggregation of all common chronic intractable problems: Chronic pain with joint instability; chronic headaches and migraines; temporomandibular joint dysfunction; dizziness or lightheadedness with standing (orthostatic intolerance); anxiety and panic disorder; irritable bowel syndrome, chronic constipation, and/or gastroparesis; and sleep dysfunction leading to chronic fatigue. Any one of these disorders by themselves can be difficult to deal with. It is typical that our patients have nearly all of them as adults.

While this list is daunting and perplexing, it can be better understood as the end result of dysfunction coming from two different systems: the musculoskeletal system and the autonomic nervous system.

Musculoskeletal System: It is easy to recognize that patients with EDS-HT have more laxity in the ligaments and tendons. As such, they are more prone to joint dislocations, subluxation, and damage to the ligaments and tendons. Arthritis can also occur, but is usually not present in the early ages, even though pain may be present.

Pain typically arises from a combination of muscle, tendon, or ligament strain. The pain can be felt in the affected structure, but it may also be perceived at the attachment site of the ligament or tendon to the bone. It is easiest to recognize this process in children who have "growing pains." The process for most children is that the laxity of the foot causes it to collapse. In response to that collapse, or pronation, the knee moves medially (toward the middle). The abductor muscles of the thigh must then pull the knee laterally (outward). This causes a pattern on pain of the outer thigh muscles, which typically is felt at night after a busy day of walking or running. In order to pull, the abductor muscles must deactivate the adductor muscles (which pull the knee inward), which is done through a nerve reflex. As a consequence of repeated deactivation, we typically see the adductor muscles become weak. This mixed pattern of tension and weakness allows the process to continue. As patients age and grow, this process of aberrant tension mixed with weakness becomes more widespread, often producing pain in the hips, back, shoulders, and neck.

While dislocations and patterns are easily visible, what is not readily perceived is that patients with EDS-HT have impaired proprioception (body awareness and ability to understand the body's position in relation to other objects). This has been studied in multiple ways and it has been demonstrated that the proprioceptive signals do not get appropriately generated with muscle tension. The brain uses the many signals of muscle tension and length to interpret body position. Since those signals are inadequate, the brain must "guess" the body's position or use other senses to compensate. Because of this, patients with EDS-HT tend to have more postural sway. Studies have demonstrated that persons with EDS-HT tend to have excessive movement of the trunk while standing still, show more movement with walking, and have difficulty recovering the body to the center of balance when they are bumped from a standing position. This additional movement of the core and instability of balance contributes to constant process of tension going on throughout the body, resulting in additional pain.

An important insight from proprioception is the way in which the signal is generated. The sensory organs that contribute to proprioception depend on the recognition of tension, which is a property that depends on tensile strength of the tissue. Since the tissue tensile strength is altered, the proprioception signals are not adequately generated.

The Autonomic System: The autonomic system is the collection of nerves that control the body's unconscious functions such as heart rate, blood pressure, breathing rate, alertness, digestion, and sleep. There are complex interactions within this system, but we can simplistically divide the autonomic system into two halves. The sympathetic nervous system controls the activation state of the body, known as the "fight-or-flight response." The parasympathetic nervous system controls the recovery state of the body, characterized as "rest and digest." The two systems work in alternation and are active at different times of the day and in different parts of the body.

What we recognize in EDS-HT, is the majority of patients with multi-system problems have orthostatic intolerance (dizziness or "blacking-out" with standing). This symptom has been correlated to over-sensitivity of the sympathetic nervous system. That system is activated easily and gives bigger responses than it should. When it is activated, the symptoms are those typically seen in the fight-or-flight response, which is also a fear reaction: Panic, anxiety, racing heartbeat, elevated blood pressure, rapid breathing, pale skin, and dry mouth. Additionally, the fight-or-flight response shuts down the parasympathetic nervous system. As such it shuts down sleep, making a person awake and vigilant. It also shuts down digestion, leading to nausea, inability to eat, and abdominal pain.

From these processes, we can see the roots of many of the associated disorders in EDS-HT. The sympathetic nervous brings about panic and anxiety, abdominal pain and nausea, and sleep impairment. These symptoms are tied to the gateway symptom of orthostatic intolerance. In some patients, this can be easily seen with standing. As the patient stands, blood follows the gravitational pull toward the feet. Normally, the system compensates for this, but patients with EDS-HT do not. As such, blood flow to the brain diminishes, causing the sensation of "blacking out." Then, the patient might faint, might have to sit very quickly, or they might develop another compensatory response—that is, when the brain perceives a lack of oxygen, it generates the fight-or-flight response. Because the fight-or-flight response increases blood pressure, the brain has its blood flow restored, but it comes at the price of a patient who feels anxious, jittery, nauseated, and has a racing heart beat. All of this happens because the patient stood up too fast.

The question, then, is why the system would behave this way. For this, we look to the tension sensors in the muscles, which we know to be dysfunctional in that they do not adequately register tension. There are similar sensory mechanisms throughout the body that also register tension. The sensor that registers tension in the arterial wall is called the baroreceptor. It seems to act similarly dysfunctional, since one of the main roles of the baroreceptor is to protect blood flow to the brain when a person stands.

The baroreceptor has two roles. One is to maintain constant blood pressure and the other is to maintain blood volume. The baroreceptor plays a role in blood volume much in the same way a gas gauge maintains gasoline volume in a car. It alerts the system when the volume is low so that the volume can be conserved or replaced. In the body, the compensatory mechanisms to low volume include the sensation of thirst, salt craving, and augmentation of the conservation of salt and water by the kidney. However, most patients with EDS-HT remain chronically dehydrated and will report that they are never thirsty. The consequence of low blood volume is the body must now make choices as to where blood flow is distributed. That can contribute to migraine headaches, abdominal pain and nausea after eating, and Raynaud's-like phenomena of cold, blue hands on a hot day. In each case, the fight or flight mechanism redirects blood away from an organ or tissue that may need it in favor of brain perfusion.

The blood control of the baroreceptor proceeds from the well-known "baroreflex." This reflex arc sends signals from the baroreceptor to the brain. The brain then sends nerve signals to the periphery, causing the release of the chemical "norepinephrine." Norepinephrine binds to its adrenergic receptors (like a key into a lock), causing arteries to constrict or squeeze down. As a result, blood is directed away from the hands and feet and back toward the brain. This baroreflex adjusts blood pressure with every heartbeat, causing small amounts of norepinephrine to be constantly released in

order to maintain fine control over blood pressure. Our model posits that the insensitivity of the baroreceptor causes a decreased release of norepinephrine. As a result, circulating norepinephrine would be lower than expected. The further consequence is that the lack of norepinephrine causes the body to try and adapt. It seems to do so by increasing the sensitivity of the adrenergic receptor system. The receptors activated more easily and give bigger responses. The unfortunate result is that the sensitivity of the fight-or-flight response also increases, because it uses the same adrenergic receptor. As norepinephrine levels remain low, the fight-or-flight response remains high. If this model sounds familiar, it is because a similar norepinephrine theory (without the involvement of the baroreceptor) has been suggested as the cause of "central pain sensitivity" in fibromyalgia, which may explain why drugs like Serotonin-Norepinephrine Reuptake Inhibitors (SNRI's) have been useful. What we know about fibromyalgia is that half or more (depending on the study) of patients with fibromyalgia also meet criteria for EDS-HT. Thus, while direct studies on this concept in EDS-HT are lacking, studies in fibromyalgia and its close relationship to EDS-HT suggest this model is on the right track.

Hormones: Hormones seem to play a role in the acceleration of symptoms in women. This is noticeable with puberty, but also with pregnancy. More specifically during pregnancy, the hormone relaxin is released and its job is to break down connective tissue. Because of this, many women report feeling progressively worse with each pregnancy. With proper attention to therapy (below) women can get

Summary of pathogenesis:

Our understanding of EDS-HT recognizes that:

1. Joint instability leads to abnormal patterns of muscle tension and weakness
2. Proprioceptive defects lead to increased body movement, which accentuates the processes of joint instability
3. Inappropriate activation of the sympathetic nervous system underlies the majority of non-joint related symptom complexes
4. Insensitivity of the baroreceptor leads to symptoms of orthostatic intolerance, chronic dehydration, and sensitization of the sympathetic nervous system.

Interpretation for Therapy:

Given this view of the pathogenesis, the therapy is straightforward but requires specific and sometimes specialized attention:

1. We must identify and address patterns of abnormal muscle movement, tension, and weakness. Exercises must be employed to reactivate and strengthen weakened muscle groups. Exercises, stretching, and other modalities should be used to reduce muscle tightening and pain.
2. We must identify and address proprioceptive defects through exercise to improve core strength, stability, and balance.
3. We must address chronic dehydration through volume expansion.
4. We must address the overactivity of the sympathetic nervous system through modalities designed to decrease sensitivity and preserve blood flow to the brain.

Therapies:

Physical therapy: Physical therapists can address the physical factors that include abnormal tension and weakness. They can also address the problems of proprioception through core strengthening and exercises to improve balance and stability. Many patients have had site-specific physical therapy (e.g. knee or back) and may complain that physical therapy "does not work for them." If the physical therapy did not adequately address the underlying problems, then the pain is likely to re-occur. The approach of a physical therapist to a hypermobile patient is also different, often characterized as an "inside out" strategy because it starts from the core. Therapists who are unaware of this disorder or its treatment strategy may produce less successful results.

Aquatic therapy is typically used as an initial strategy for those who are unable tolerate upright exercise due to pain or autonomic symptoms. Its advantage is the ability of buoyancy to reduce pain on the joints.

Exercise: The most successful modality for the treatment of autonomic dysfunction has proven to be a specific exercise protocol (the "Levine Protocol") developed through UT Southwestern. Their rationale for exercise is that the cardiac output in patients with POTS (a specific form of autonomic dysfunction) is low, so their solution was to improve cardiac output. Our model also considers the fact that after 20 minutes of exercise, norepinephrine will be released into the bloodstream from muscle stores. In this way, circulating norepinephrine is increased, which activates the adrenergic receptors. Now the system perceives that there is too much adrenergic activity and that allows the sensitivity of the adrenergic system to fall. When this happens, we expect the symptoms tied to the fight-or-flight response to similarly decrease.

However, most EDS-HT patients will initially reject the concept of exercise as they have found exercise to be "harmful" to them. It exacerbates pain and triggers the fight-or-flight response, leading to racing heartbeat, nausea, exhaustion, and a "sense of doom" within 10 minutes of starting exercise. The problem is that most patients consider exercise to be an activity done while standing: running, stair-climber, elliptical, Zumba, etc. If a patient is unable to protect blood to their brain while standing, they similarly cannot do so while exercising. As such, the brain continuously releases the fight-or-flight response and this appears to sabotage the benefits of exercise.

The Levine protocol specifically addresses the aspect of orthostatic intolerance by having patients sit while exercising or to exercise in a pool. When seated, the blood does not gather in the feet in the same way and the blood meets resistance to flow at the level of the hips. In the pool, the water pressure applies compression to the body, redirecting blood flow toward the brain. In both cases, blood perfusion of the brain is preserved and exercise can be performed without interference. Seated exercises include recumbent bicycle, rowing machine, and NuStep. The studied water-based exercises include swimming or kickboarding, but some of our patients have also found benefit with walking or running through the pool, as well as water aerobics.

The basics of the Levine protocol are for the patient to work up to 5 days a week, 30 minutes per day, with heart rate at 80% of its maximum (calculated by 220 minus age and multiplied by 80%). At the end of three months their study demonstrated decreased orthostatic intolerance, increased circulating blood volume, and increased cardiac output. Efficiency of the adrenal hormonal response was also improved suggesting that the feedback from the baroreceptor had improved. This agrees with other studies that have demonstrated that baroreceptor sensitivity improves following an exercise

program. Coincident with the physiologic improvements, patients also reported increased quality of life. This was compared to a control group of patients who received traditional medication for three months. The control group also noted less dizziness with standing, but showed no other physiologic improvement and no change in quality of life.

Our experience in the Connective Tissue Clinic is that before we routinely advised exercise, our patients would typically return to report that our interventions helped them feel "less bad." Only when we started patients exercising did we see patients return to the clinic to use the phrase "I feel good." When they discontinue exercise (for various reasons) symptoms return. This means that exercise must be adopted not as a short term therapy, but rather, as a way of life. The result has been so successful that some of our patients have been able to transition off of disability and we have been able to resolve the symptoms of other patients to where they no longer need our services.

The central tenet of therapy for EDS-HT is that the goal of any medical intervention is to improve adherence of the patient to an aerobic exercise program.

Fluid Intake: Because the thirst response is dulled and because the kidneys do efficiently resorb fluid, patients must be advised to drink more than expected and to do so even if they "do not feel like it." The typical goal is 90 to 100 ounces of all fluids per day. Salt should also be increased to approximately 3 to 5 grams of additional salt added to the food. This is roughly 2/3 to 1 full teaspoon of salt.

Other autonomic management:

Medications are sometimes used, but should be seen as additions to the increased fluid intake and exercise, not substitutions. IV fluids are sometimes administered on a periodic basis, but should be seen as a measure of last resort and their use limited. Medications to improve fluid resorption, such as fludrocortisone have been used in patients with autonomic dysfunction. Diuretics, including spironolactone, should be avoided where possible. Midodrine, an adrenergic agonist, helps redirect blood flow away from the periphery and toward the brain. It can cause high blood pressure when lying down, so is typically used during the day, but not at night.

Labile fluctuating blood pressure, ranging from low to high, can be seen in patients with EDS-HT. It can be understood as a baseline problem of low blood pressure with spikes of high blood pressure being due to the sympathetic nervous system activation. Treatment with diuretics may cause this to become worse. Volume expansion and, if necessary, beta blockers offer a more rational approach.

Beta blockers are the traditional therapy for autonomic dysfunction, as they reduce the symptoms from the sympathetic nervous system. However, they mask but do not address the underlying cause. Some patients will experience depression or augmented hypotension as side effects. Some patients on beta blockers will also experience greater mast cell-related symptoms (see histamine, below), as norepinephrine suppresses mast cells whereas beta blockers allow them to remain active. Because of these effects, we typically do not use beta blockers as first line therapy for orthostatic intolerance. However, we have noted that some patients have improved sleep with beta blockers, as there is less sleep disruption from the fight-or-flight system. As such, overnight usage to help improve symptoms of chronic fatigue can be helpful.

Histamine control: Some patients will note more episodes of flushing, hives, itching, and diarrhea in response to foods or environmental allergies. These responses are caused by histamine, which is released by mast cells. Histamine causes blood vessels to dilate and become leaky. Both of these effects counteract the goals of volume expansion and can exacerbate autonomic symptoms. Some patients have noted improvement of their overall symptoms, including irritable bowel, with daily over-the-counter dosing of Zyrtec and Zantac. Other medications may be needed and we typically work with allergists when Zyrtec and Zantac are insufficient.

Some patients have overactive responses due to "mast cell activation syndrome," which is a condition in which the mast cells respond inappropriately to many different triggers. Other patients seem to have traditional allergies, but the allergies are more vigorous. Whatever the cause, it seems reasonable to aggressively suppress allergy symptoms as they may impact the autonomic system.

Avoidance of triggers is another important component. Some foods may be trigger symptoms, but one should remember that medications, especially narcotics, can trigger histamine release.

Pain Medications: Pain management typically proceeds along the same lines as fibromyalgia, given the close relationship. We often start with simple medications, such as ibuprofen, acetaminophen, or naproxen. After that, medications such as Lyrica, Neurontin, Elavil, Cymbalta, or Savella might be used. We do not recommend round-the-clock usage of narcotics or muscles relaxers, as these decrease muscle tone, which defeats the purpose of physical therapy. We often refer pain management clinics when simple solutions are not working. However, primary physicians who treat fibromyalgia may well be able to manage pain medications as well.

Surgical Concerns:

Joint Capsule tear: Shoulder or hip labral tears can produce chronic irritation and pain. The goal is reduce the pain associated with these tears. "Tightening the joints" typically does not last as long as expected unless special precautions are taken to secure the joint. Having a surgeon familiar with such differences is important. However, both physician and patient need to be aware of the lower expectations for these procedures.

Cervical instability: Neck instability is common and can respond to physical therapy. This remains our first choice of intervention. If there is intractable neck and head pain or signs of neurologic compression, stabilization through fusion may be necessary. However, one should be warned that fusion at one vertebral level may lead to instability of segments above and below.

Chiari malformation: The association of EDS with Chiari malformation (in which the hindbrain and cerebellum are compressed into the opening at the base of the skull) has been reported in the literature, but the magnitude is unclear. The diagnostic workup varies according to regional resources. Some neurosurgeons require an upright MRI (which is not available in Ohio) whereas others prefer cine-flow studies. The decision to pursue surgery is often based on symptoms of autonomic dysfunction which can be explained by other factors. Thus, we recommend fully treating autonomic dysfunction as above before actively pursuing surgical evaluation.

Conclusion: Ehlers Danlos Hypermobility Type is a common disorder of connective tissue. Left unchecked, the condition can produce considerable disability. However, with proper awareness and effort, the disease process can be improved and overcome.