

A woman in a blue patterned top and light blue leggings is performing a handstand on a dark brown leather couch. She is looking down at her smartphone. A white coffee cup on a saucer is on the floor in front of her. The background is a plain wall.

Hypermobility Spectrum Disorders

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Who Am I?



- Professor Emeritus, Physical Therapy, Clarkson University.
- Staff PT, St. Lawrence Health System, Potsdam NY.
 - Clinical specialties: hypermobility, chronic pain, fibromyalgia, headaches, temporomandibular disorders
 - I treat through Lawrence Ave Physical Rehab office, 315-261-5460
- Facilitator of the North America Allied Health Professionals ECHO
- Member of:
 - The Allied Health Working Group of the International Consortium of Ehlers-Danlos Syndromes and Hypermobility Spectrum Disorders
 - Past member of The National Academy of Sciences, Engineering and Medicine Committee on Selected Heritable Connective Tissue Disorders and Disability.
- Author of many articles related to HSD/hEDS
- Author of “Chronic Pain” chapter in *Physical Rehabilitation* textbook for PT students
- Lrussek@Clarkson.edu
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**I do not have any
conflicts of interest to report**

Objectives

By the end of this session, participants will be able to:

1. Describe how Hypermobile Spectrum Disorders presents
 - Describe presentation of common comorbidities: Postural Orthostatic Tachycardia Syndrome (POTS) and Mast Cell Activation Syndrome (MCAS)
2. Outline an approach to identifying problem areas in these patients
3. Outline a management approach to Hypermobile Spectrum Disorders and the “Trifecta” of HSD/POTS/MCAS
4. Access useful resources for managing these patients

Patient handouts on my website

<https://webpace.clarkson.edu/~lrussek/research.html>





Why the Zebra?

- Most health professionals have learned: “When you hear hoofbeats, look for horses, not zebras.”
- But people with HSD *are* different, and they need to be treated differently.
- Treating a zebra as though it were a horse does not work well.
- “Why Zebras are not Horses” information sheet for PTs:
<https://webpace.clarkson.edu/~lrussek/docs/hypermobility/ZebraNotHorses.pdf>



NASEM Guide Statement on Delayed Diagnosis of Heritable Disorders of Connective Tissues (HDCT)

- *"Delayed or misdiagnosis of individuals with HDCTs can result in*
 - *inappropriate medical interventions;*
 - *inability to accurately assess the risks and benefits associated with medical procedures;*
 - *inability to access necessary reasonable accommodations at work or school;*
 - *family stress and dysfunction;*
 - *stress associated with unexplained and repeated evidence of trauma, leading to inappropriate suspicion of child abuse;*
 - *inappropriate assessments and incorrect diagnoses; and*
 - *mistrust of health care providers and negative expectations for future health care encounters"*
- <https://nap.nationalacademies.org/catalog/26431/selected-heritable-disorders-of-connective-tissue-and-disability> (page 296)
- In adults increases pain, disability and burden of the disorder
- In children is associated with poor pain control, functional deficits, and interference with school (Kalisch, 2019; Adib, 2005)

For the Primer, visit doi:10.1038/s41572-020-0194-9

➔ The Ehlers–Danlos syndromes (EDS) are a group of connective tissue disorders caused by alterations in genes encoding fibrillar collagens, collagen modifying or collagen-processing enzymes, or enzymes that modify glycosaminoglycans within the extracellular matrix (ECM).

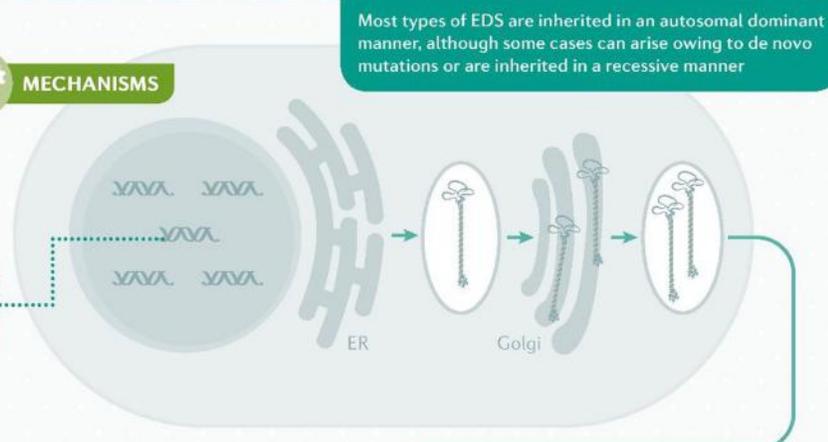
Variants in genes encoding the fibrillar procollagens I, III and V, or in genes encoding enzymes responsible for cleaving procollagen to mature collagen, lead to collagen fibrils with an abnormal structure or composition

DIAGNOSIS

The symptoms of EDS are diverse and differ between subtypes. Symptoms that are found in multiple EDS subtypes include joint hypermobility, soft and hyperextensible skin, poor wound healing, pain and easy bruising. Vascular and musculoskeletal symptoms are present in some subtypes. Diagnostic work-up comprises clinical examination, followed by genetic testing in individuals who fulfil the clinical criteria for an EDS subtype. Genetic testing can include targeted analysis in those with a family history of EDS caused by a known genetic variant or, more frequently, next-generation sequencing using multi-gene panels. Genetic diagnosis should lead to family testing to enable detection of EDS in family members and, for patients with a recessive form of EDS, carrier testing in their partners to evaluate the risk of transmission to offspring. Of note, the genetic cause of hypermobile EDS has not been determined and, therefore, diagnosis of this condition is based on the presence of clinical manifestations only.

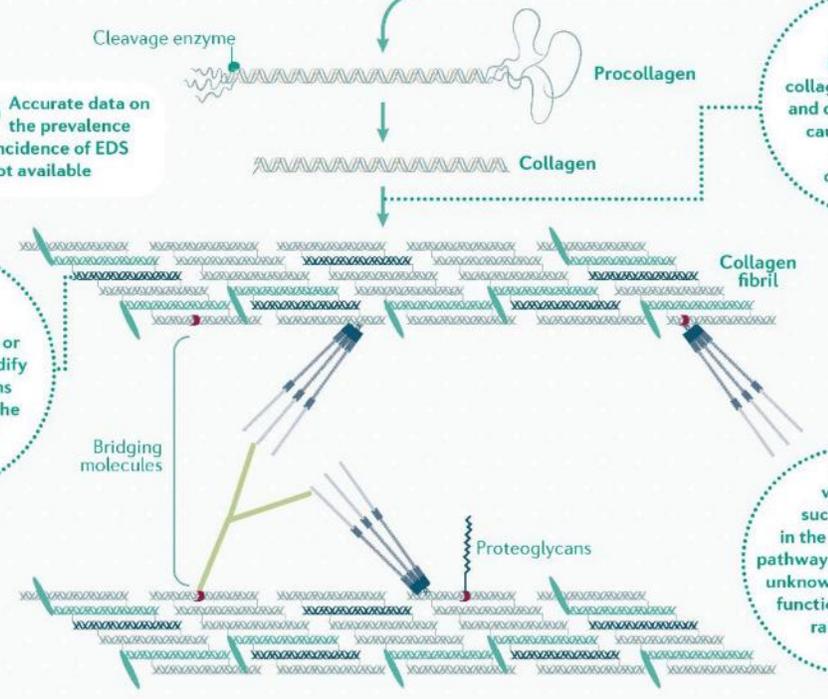
Variants in genes encoding ECM bridging molecules or in enzymes that modify ECM proteoglycans can interfere with the organization of collagen fibrils

MECHANISMS



Most types of EDS are inherited in an autosomal dominant manner, although some cases can arise owing to de novo mutations or are inherited in a recessive manner

! Accurate data on the prevalence and incidence of EDS are not available



MANAGEMENT

All patients with EDS should receive multi-disciplinary care and, if available, be part of a patient advocacy community. The precise treatment depends upon the subtype of EDS and its manifestations. Physiotherapy is essential for patients with musculoskeletal alterations. Helmets and/or skin protection, or joint protection, braces or splints can be used to reduce the risk of injury in patients with skin fragility or joint hypermobility. In addition, low-resistance exercise (such as walking or swimming) can improve joint stability, although exercise that place considerable strain on the joints (such as gymnastics or weight lifting) should be avoided. Monitoring for cardiovascular alterations using non-invasive procedures is recommended in patients at risk of adverse cardiovascular events.

Variants in genes involved in collagen crosslinking and collagen folding causes impaired collagen crosslinking

Other variants, such as those in the complement pathway and in genes of unknown intracellular function, can cause rarer forms of EDS

OUTLOOK

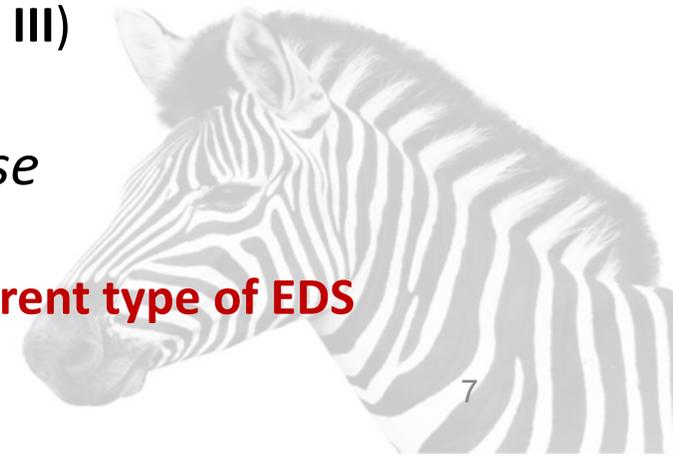
Despite improvements in genetic testing, some forms of EDS (hypermobile EDS) and some patients with other forms of EDS have no identified genetic cause, which can hinder diagnosis of these conditions. Large-scale international studies are underway to address this issue. Genotype–phenotype correlations for EDS are only starting to emerge; additional correlations may be identified by ongoing research.

Pathophysiology (for reference)

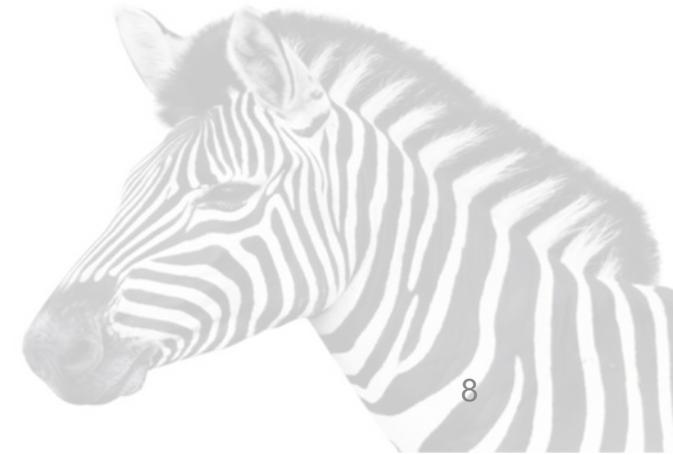


Types of EDS and Hypermobility

- Generalized joint hypermobility (GJH): asymptomatic widespread hypermobility
- Ehlers-Danlos syndrome (EDS)
 - Heterogenous group of heritable connective tissue disorders
 - In 2017, new classification of EDS (Malfait, 2017)
 - 13 subtypes
- Hypermobile EDS (hEDS) and Hypermobility Spectrum Disorders (HSD)
 - Pre 2017 terminology:
 - (Benign) Joint hypermobility syndrome (**BJHS, JHS & HMS**)
 - Ehlers-Danlos Syndrome – hypermobility type (**EDS-HT or EDS-type III**)
 - Most common subtype (~90% of EDS)
 - hEDS/HSD is the only EDS subtype with *no known genetic cause*
 - Diagnosis remains clinical
 - **Genetic testing is NOT generally helpful unless you suspect a different type of EDS**



Classical EDS



Vascular EDS

RECOGNIZING THESE SIGNS
"WILL SAVE LIVES"
"A diagnosis...CAN defuse this silent genetic time bomb!"



Common Appearance?

- Translucent thin skin with visible veins especially on face/chest/abdomen*
- Early onset varicose veins*
- Unusual bruising without cause*
- Attached earlobes
- Narrow palate
- Deep-set or almond shaped eyes

**Note, these signs may be present in hEDS, usually less dramatic*

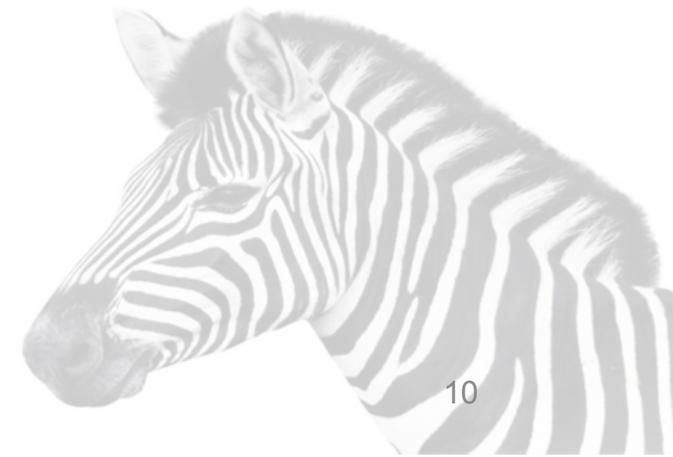


Russek: Hypermobility

www.ehlersdanlosnetwork.org/vascular.html
<https://www.pinterest.cl/pin/558868634993169756/>
<https://www.annabelschallenge.org/vascular-eds>

How Common is Hypermobility?

- hEDS/HSD is the most common systemic inherited connective tissue disorder in humans. (Tinkle, 2017)
- Overall prevalence of symptomatic HSD in US: 1-3%
- hEDS/HSD in healthcare: (Simmonds, 2022; To, 2017)
 - 37% of adult patients in rheumatology clinics
 - 39% of adult patients in pain clinics
 - 30% of adult patients in primary care clinics
 - 21% of pediatric PT patients



THE BEIGHTON SCORING SYSTEM

Measuring joint hypermobility

A. 5th FINGER / 'PINKIES'

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

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

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



B. THUMBS

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

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



D. KNEES

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

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



C. ELBOWS

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

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

E. SPINE

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

If yes, add **one point**.



Diagnosis: Adults

2017 hEDS Criteria

hEDS was defined for the purpose of seeking a genetic marker for hypermobile EDS

hEDS Must meet all 3 criteria:

1. Generalized joint hypermobility
2. Two of the following:
 - A. $\geq 5/12$ Features of inherited connective tissue disorder
 - B. Family history
 - C. Musculoskeletal pain > 3 months, or dislocations
3. Absence of exclusion criteria
(there isn't another good explanation)

- These replace both Brighton and Villefranche Criteria for JHS, HMS, EDS-HT, EDS-type III
- **These hEDS diagnostic criteria are problematic for several reasons, and do not alter PT for HSD**



Diagnostic Criteria for Hypermobile Ehlers-Danlos Syndrome (hEDS)
This diagnostic checklist is for doctors across all disciplines to be able to diagnose EDS



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

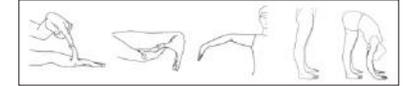
The clinical diagnosis of hypermobile EDS needs the simultaneous presence of all criteria, **1 and 2 and 3**.

CRITERION 1 – Generalized Joint Hypermobility

One of the following selected:

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

Beighton Score: ____/9



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

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

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

Feature A (five must be present)

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

Feature A total: ____/12

Feature B

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

Feature C (must have at least one)

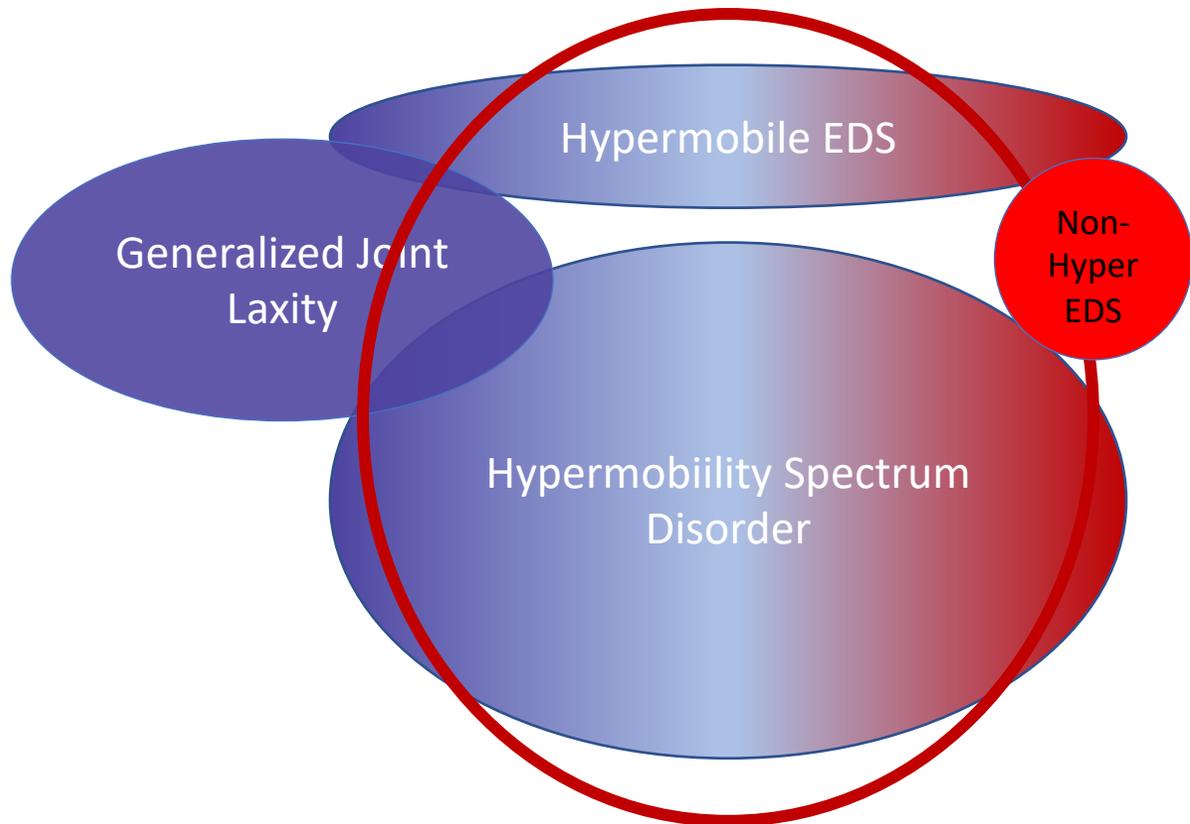
- Musculoskeletal pain in two or more limbs, recurring daily for at least 3 months
- Chronic, widespread pain for ≥ 3 months
- Recurrent joint dislocations or frank joint instability, in the absence of trauma

CRITERION 3 – All of the following prerequisites MUST be met

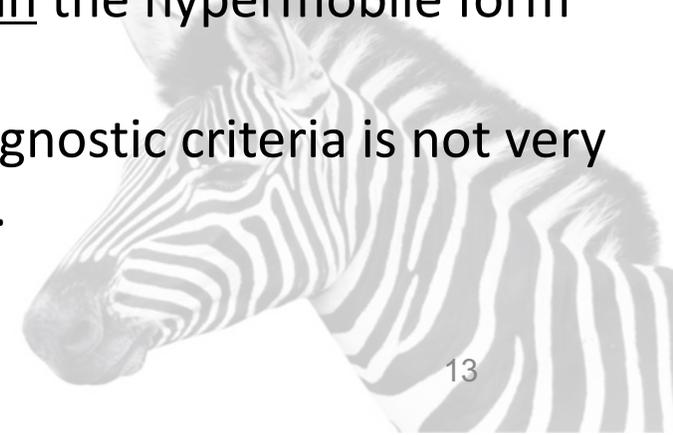
1. Absence of unusual skin fragility, which should prompt consideration of other types of EDS
2. Exclusion of other heritable and acquired connective tissue disorders, including autoimmune rheumatologic conditions. In patients with an acquired CTD (e.g. Lupus, Rheumatoid Arthritis, etc.), additional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

HSD vs. hEDS

Asymptomatic Mild Symptoms Severe Symptoms



- hEDS if all checklist criteria are met
- HSD for “*all individuals who present with complaints and/or life quality limitations because of joint hypermobility*” (Castori, 2017)
- Pain, symptoms, & disability are similar for both groups – one is not worse than the other
(Copetti, 2019; Aubry-Rozier, 2021)
 - Patients who are hypermobile and have problems related to their hypermobility, have HSD/hEDS
- Genetic testing is not helpful unless you suspect a form of EDS other than the hypermobile form (HSD/hEDS)
- So... using the hEDS diagnostic criteria is not very helpful for patient care.



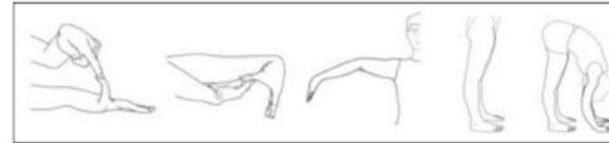
2023 Joint Hypermobility Criteria for Children

Five key questions to ask:

1. Generalized joint hypermobility
 - a. Beighton Score ≥ 6
2. Skin and Tissue Abnormalities
 - a. 3 out of 6 criteria \rightarrow skin involvement subtype
3. Musculoskeletal complications
 - a. 2 out of 3 criteria \rightarrow HSD
4. Co-morbidities
 - a. Yes \rightarrow co-morbidities subtype
5. Excluding other conditions
 - a. Patient's symptoms caused by other conditions

(Tofts, 2023)

Children From 5 Years Of Age Until Biological Maturity



L R L R L R L R

Beighton Score: ____/9
Must be a minimum of 6

Skin and Tissue Abnormalities

- Unusually Soft Skin – unusually soft and/or velvety skin
- Mild Skin extensibility
- Unexplained striae distensae or rubae at the back, groin, thighs, breasts and/or abdomen without a history of significant gain or loss of body fat or weight
- Atrophic scarring involving at least 1 site and without the formation of truly papyraceous and/or haemosideric scars as seen in classical EDS
- Bilateral piezogenic papules in the heel
- Recurrent hernia, or hernia in more than one site (excludes congenital umbilical hernia)

Score: ____/6
Must be a minimum of 3

Musculoskeletal Complications

- Episodic Activity related pain not meeting the chronic pain frequency and duration criteria
- Recurrent joint dislocations, or recurrent subluxations in the absence of trauma, and/or frank joint subluxation on physical exam in more than one joint (excludes radial head <2yrs)
- Soft tissue injuries – One major (needing surgical repair) and/or current multiple minor tendon, and/or ligament tears

Score: ____/3
Must be a minimum of 2

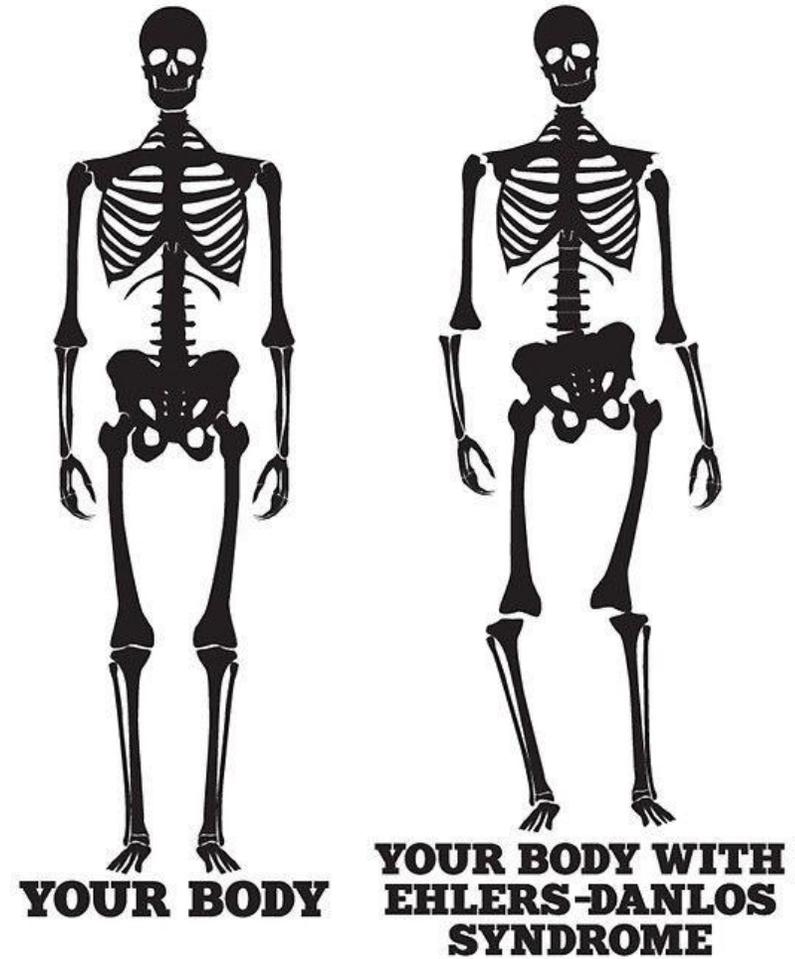
Co-Morbidities

- Chronic primary pain
- Chronic fatigue
- Functional GI disorders
- Functional bladder disorders
- Primary dysautonomia
- Anxiety

Any number causing
distressor disability?
Y / N

Clinical Presentation & Common Comorbidities

**“The Terrible
Trifecta”**



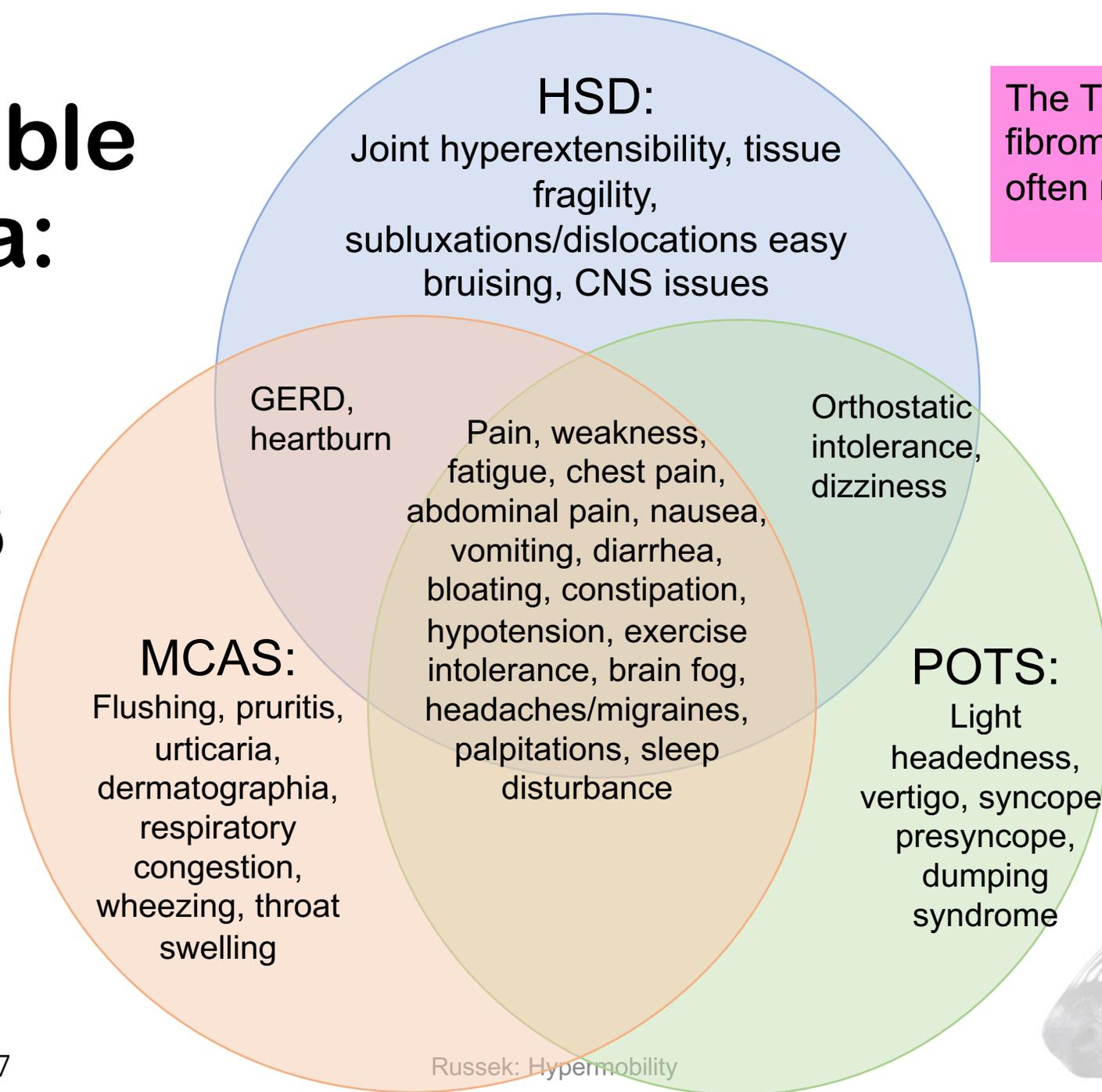
ehlersdanlos

Presentation & Comorbidities

- **Musculoskeletal:** joint instability, joint pain, soft tissue injury, muscle spasm/trigger points, scoliosis, decreased bone density
- **Gastrointestinal:** GERD, IBS with diarrhea and/or constipation, painful bloating, gastroparesis, nausea/vomiting, prolapse, hernias
- **Autonomic nervous system:** dysautonomia (POTS or orthostatic intolerance), fatigue, dizziness, Raynaud's, exercise & heat intolerance
- **Neurological:** proprioceptive deficits, interoceptive deficits, clumsiness, headache, migraine, nerve compression, central sensitization, cervicomedullary syndrome, Chiari, Tarlov cysts, CSF leaks, tethered cord
- **Cardiopulmonary:** dysfunctional breathing, bleeding disorders, varicose veins, mitral valve prolapse, pelvic congestion
- **Mental health:** anxiety, panic disorder, depression, brain fog.
- **Neurodevelopmental:** developmental co-ordination disorder, motor delay, autistic spectrum disorder, attention deficit hyperactivity disorder
- **Immunologic:** MCAS, rashes, hives, chemical and food sensitivities, excessive inflammatory response, persistent fatigue, GI dysfunction, migraine
- **Dermatologic:** hyperextensible skin, fragile skin, poor wound healing, easy bruising
- **Urogenital:** incontinence, UTI, interstitial cystitis, dysmenorrhea, pelvic pain, vulvodynia, painful intercourse, prolapse
- **Multisystemic:** chronic fatigue, sleep disorder, brain fog



The Terrible Trifecta: HSD POTS MCAS



The Trifecta looks a lot like fibromyalgia, and is probably often misdiagnosed as FM (Russek, 2018)

Mast Cell Activation Syndrome/Disorder

Postural Orthostatic Tachycardia Syndrome



Dysautonomia (especially POTS)

Overview of
POTS

PUPILOMOTOR
impaired pupil response
(uncomfortable in bright light)
difficulty with vision

NEUROLOGICAL
migraine, cognitive
deficits, brain fog &
mental clouding

SECRETOMOTOR
difficulty sweating, tearing
and other fluid production
(dry eyes, dry mouth,
difficulty swallowing, dry skin)

PULMONARY
shortness of breath
easily winded
difficulty breathing

GASTROINTESTINAL
nausea, vomiting, diarrhea,
constipation, abdominal
pain, reflux, heartburn,
impaired motility

CARDIOVASCULAR
palpitations, chest discomfort
high heart rate (tachycardia)
low heart rate (bradycardia)
high or low blood pressure
abnormal blood vessel functioning
blood pooling

URINARY
difficulty with urine
retention and/or excretion

ORTHOSTATIC INTOLERANCE
difficulty standing still, fatigue, lightheadedness,
increase in symptoms with upright posture,
fainting (syncope) or near-fainting, pallor

Symptoms can be
SUDDEN and
unpredictable
in onset

- HSD is a risk factor
- Common triggers:
 - Puberty
 - Concussion
 - COVID
 - Deconditioning
 - Sleep disorders
- 62% of kids with POTS have HSD/hEDS
- 1/3 of patients develop POTS symptoms before age 18
 - Median age 13.1 yrs
 - Female:male ratio is 5:1

Boris, 2021; Chen, 2020; Zhang, 2020

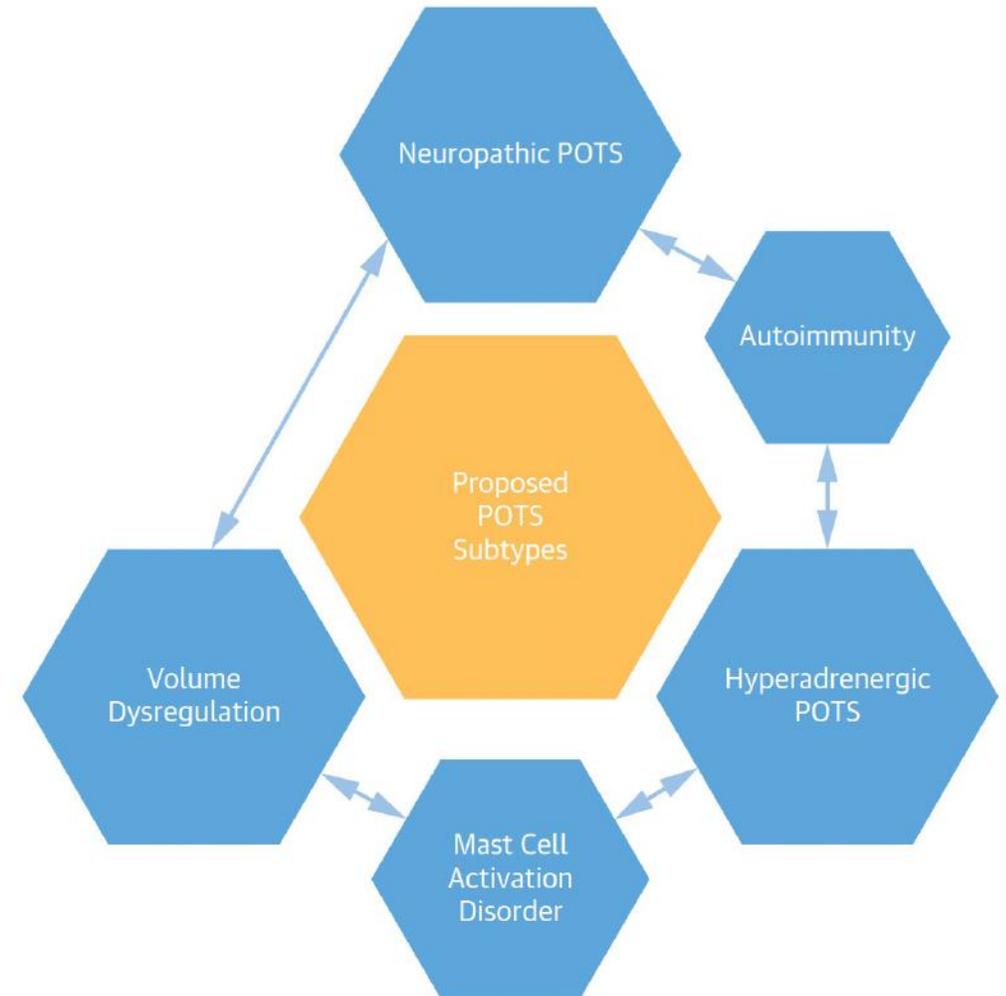
Types of POTS

- Volume dysregulation (30%)
 - Due to stretchy veins, pooling
 - Maybe common in HSD?
- Neuropathic POTS (>50%)
 - Decreased autonomic nerve function
 - Less anxiety & depression, ↓ sweating
 - Maybe associated with neck problems?
- Mast Cell Activation (controversial)
 - Flushing, short of breath, headache, lightheaded, ↑ sweating, GI symptoms
 - Maybe contributes to POTS & HSD?
- Hyperadrenergic (30-60%)
 - Palpitations, tremulous, sweating, nausea
 - Increased by exercise & stress
- People may have multiple types or switch among different types
- Non-pharmacological management probably the same

(Bryarly, 2019)

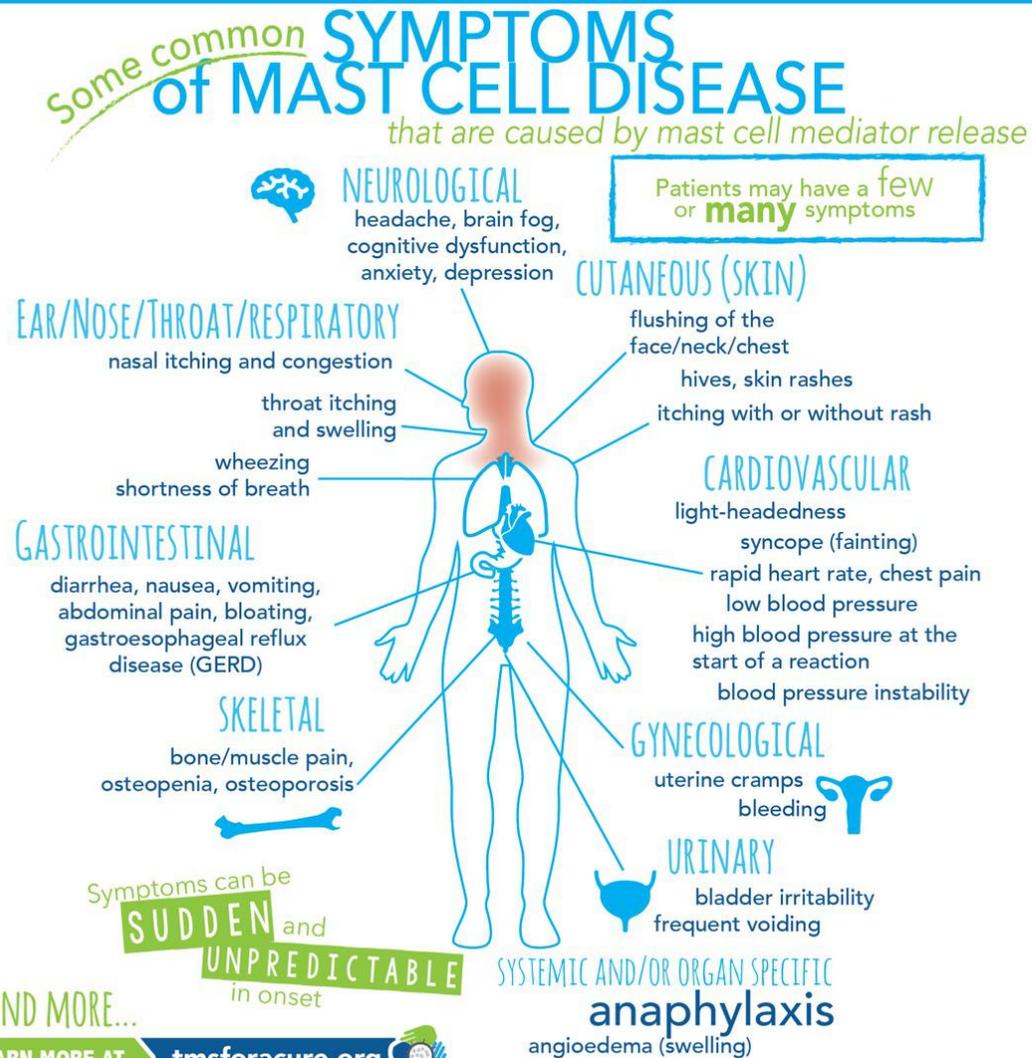
Russek: Hypermobilit

FIGURE 3 POTS and Proposed Subtypes



Several subtypes of POTS have been proposed and include neuropathic POTS, autoimmunity, hyperadrenergic POTS, mast cell activation disorder, and volume dysregulation. These subtypes are not mutually exclusive or clearly independent. POTS = postural orthostatic tachycardia syndrome.

Mast Cell Activation Syndrome (MCAS)



Lab testing has very, very high false negative rates

- Possible 17% of people in US
- Diagnosis
 1. Allergy symptoms and other symptoms in two or more organ systems that keep coming back or are chronic
 2. Higher than normal levels of tryptase, histamine, or prostaglandins in your blood
 3. Getting better after using antihistamine medications or other drugs that block chemicals released by mast cells
- Can also use “Validated MCAS Questionnaire” (Afrin, 2014)

Chronic Fatigue

- May be due to
 - POTS/dysautonomia
 - Propranolol may aggravate fatigue, cold hands/feet, difficulty sleeping
 - Deconditioning
 - Malnutrition due to GI problems from HSD, POTS, or MCAD
 - Sleep dysfunction due to POTS or pain from HSD
 - Stress from medical/health issues
 - MCAS

Hakim, 2017



GI Dysfunction

- HSD, POTS and MCAS can all cause different GI problems
 - HSD: gastroparesis, constipation, median arcuate ligament syndrome (MALS), superior mesenteric artery syndrome (SMAS)
 - POTS: Dumping syndrome
 - MCAS: IBS, food/med sensitivities
- Check for physical reasons for disordered eating before diagnosing “eating disorders”

Blajwajs, 2023;

Lam, 2023;
Russek:

MCAS

Table 2 Summary of the main foregut gut–brain disorders, key features, management options and optimal nutrition approach

Foregut gut–brain disorder diagnosis	Key features	Diagnostic basis and tests	Management options	Optimal nutrition approach
Oesophageal dysmotility	Difficulty swallowing	Abnormalities on high resolution manometry	Dietary adjustment and eating behavioural modification.	Oral nutritional supplements if needed. NG feeding if malnourished.
Rumination syndrome	High pressure gastric contractions precede regurgitation/vomiting	Typical history. Concurrent impedance/manometry with meal provocation	Diaphragmatic breathing, baclofen, Nissens fundoplication (selected patients)	Optimised effortful oral feeding, short term bridging NJ to therapies only if malnourished
Cyclical vomiting syndrome and cannabis hyperemesis syndrome	Bouts of hyperemesis with intervals of normality. History of migraines. Relief from hot baths.	Clinical history is typical. Exclusion of other structural or central neural causes	May respond to tricyclics and migraine prophylaxis. Abstinence from cannabis.	Short bouts may need parenteral fluids/electrolytes. NJ likely to be unstable and unnecessary.
Chronic nausea and vomiting	Low-grade background constant nausea and vomiting	Clinical history and exclusion of other structural or central neural causes	Prokinetics, antiemetics, gut–brain neuromodulators	Optimised effortful oral feeding, avoid NJ unless malnourished.
Functional dyspepsia and gastroparesis	Overlapping spectrum of varying degrees of sensorimotor impairment of gastroduodenal function	Clinical history and solid meal gastric emptying test off medication affecting gastric emptying (but not based on gastric emptying study alone)	Pain management (avoid opioids), psychosocial support, buspirone, gut-brain neuromodulators including mirtazapine, pro-kinetics.	If malnourished with predominantly gastric muscle failure (gastroparesis), then trial of NJ with view to longer term post-pyloric feeding tube.
CIPO and enteric (small bowel) dysmotility (ED)	Non-mechanically obstructed dilated small bowel (CIPO) or significantly abnormal small bowel manometry or transit (ED)	CIPO—dilated small bowel radiologically. ED—small bowel manometry or abnormal transit. Full thickness biopsy if undergoing venting surgery.	Prokinetics, small intestinal bacterial overgrowth therapy, non-opioid analgesia with gut–brain neuromodulators	CIPO more likely to need parenteral nutrition than ED which should be manageable with optimised effortful oral or enteral feed.
Centrally mediated abdominal pain and narcotic bowel syndrome (NBS)	Chronic continuous abdominal pain with neuropathic features. Escalating opioid doses in NBS.	Clinical history and exclusion of other causes.	Non-opioid analgesics (eg, duloxetine). Opioid stabilisation and reduction. Mu-opioid antagonists.	Avoid enteral tube and parenteral feeding.
Somatoform disorder/central sensitivity syndrome	Overlapping multiple functional symptom syndromes	Psychiatric evaluation	Clinical psychology/ liaison psychiatry. Central neuromodulators	Avoid iatrogenesis due to escalating invasive approaches.
Avoidant restrictive food intake disorder	Restrictive and avoidant behaviours not body image driven, but anxiety, fear, food related symptom and fixed (eg, health) beliefs	Psychiatric evaluation.	Clinical psychology and liaison psychiatry input	If severely malnourished may need short-term bridging enteral tube feeding to therapies but need not be post-pyloric.

CIPO, chronic intestinal pseudo-obstruction; ED, enteric dysmotility; NBS, narcotic bowel syndrome; NG, nasogastric; NJ, nasojejunal.

Bleeding Disorders

- 62% of EDS (mixed types) patients had bleeding disorders
 - Easy bruising
 - Hematomas
 - Menorrhagia
 - Oral bleeding, minor wounds, nose bleeds
 - Excessive surgical bleeding, post partum bleeding
 - GI bleeding, NSAID bleeding, hematuria, hemarthrosis
- International Society of Thrombosis and Haemostasis bleeding assessment tool (ISTH-BAT)
 - Scores >5 are abnormal in adult women
- 14% of patients with EDS reported menorrhagia that was life threatening or required surgery

Kumskova, 2022



Neurological Signs & Symptoms

- Pseudo seizures/non-epileptic seizures, fainting and dystonia (muscle spasticity) may be due to cervical instability. (Russek, 2022)
 - Cervical instability may be aggravated by an MCAD flare
 - MRI done with patient lying down and the neck in neutral cannot diagnose cervical instability
- Fainting caused by POTS-related syncopal events can mimic seizures, especially when they include myoclonic jerking (spastic twitching of muscles). (Rugg-Gunn, 2009)
- People with HSD are more vulnerable to a variety of neurological conditions:
 - Craniocervical and atlantoaxial instability (CCI and AAI), Chiari I malformation, CSF (cerebrospinal fluid) leaks, idiopathic intracranial hypertension, Eagle syndrome, tethered cord and Tarlov cysts. (Henderson, 2017)
- Patients may be anxious because of these symptoms, but this doesn't mean their symptoms are caused by anxiety
- Functional Neurological Disorders (FND) is a condition where the nervous system malfunctions. FND can exist in HSD, but look for other explanations first.

Psychological Comorbidities

- Anxiety
- Depression
- Attention deficit hyperactivity disorder
- Autism spectrum disorder
- Eating disorders/disordered eating
- Sleep disorders
- POTS and MCAS also have increased risk of anxiety, ADHD, eating disorders, sleep disorders
- Do not interpret psychological issues as ‘somatization’ or ‘functional’ disorders

De Vries, 2021; Blajwajs, 2023; Bulbena-Cabré, 2023; Bulbena, 2023; Eccles, 2022; Kindgren, 2021

Gender Dysphoria

- A study of 166 adolescents with EDS of HSD
 - 17% reported gender dysphoria, of these:
 - 61% reported gender as 'transgender'
 - 14% reported as nonbinary
 - 47% preferred he/him pronouns, and 39% preferred they/them pronouns

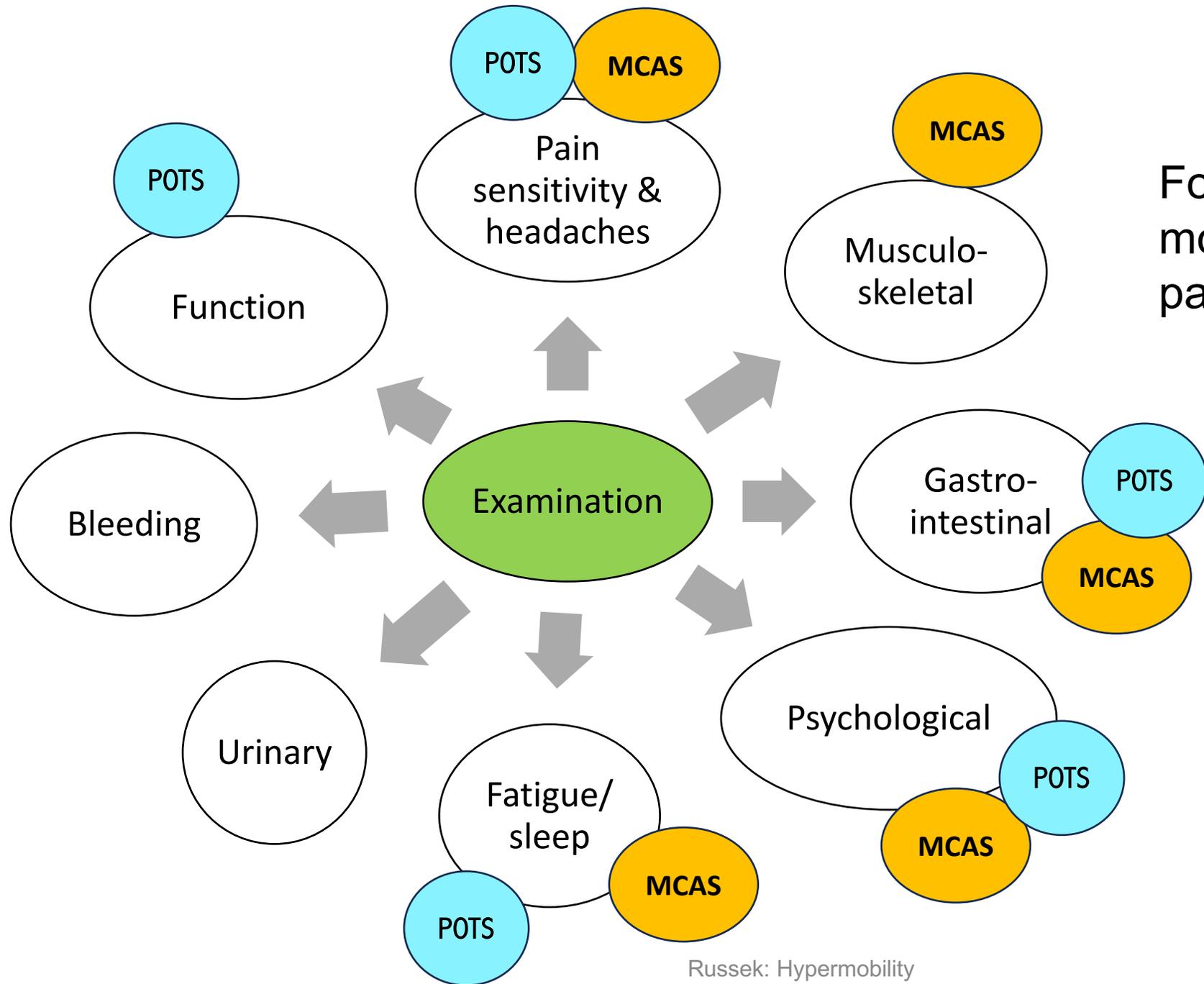
(Jones, 2022)
- A case series of patients transitioning from female to male
 - 3 patients had decreased POTS symptoms with testosterone therapy

(Boris, 2019)





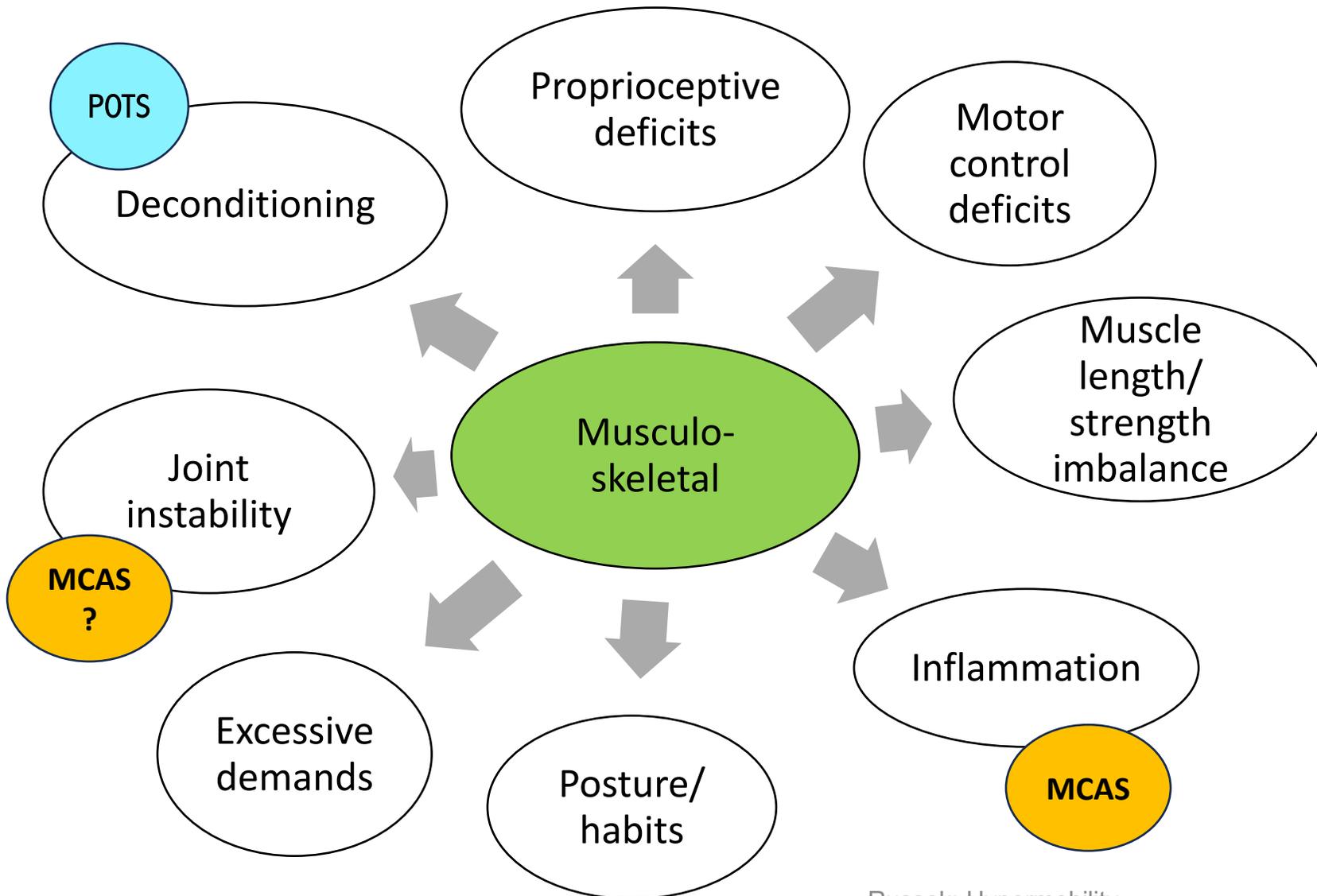
(Physical Therapy) Examination of Patients with HSD



Focus on what is most important to the patient/family



Musculoskeletal & Function Problems



Address contributing factors

- Posture, standing and sitting
- Segmental alignment, including chronic subluxations
- Joint laxity, accessory movements, range of motion
- Proprioception/motor control
- Muscle tightness
- Strength
- Endurance (muscular and/or cardiovascular)
- Autonomic function

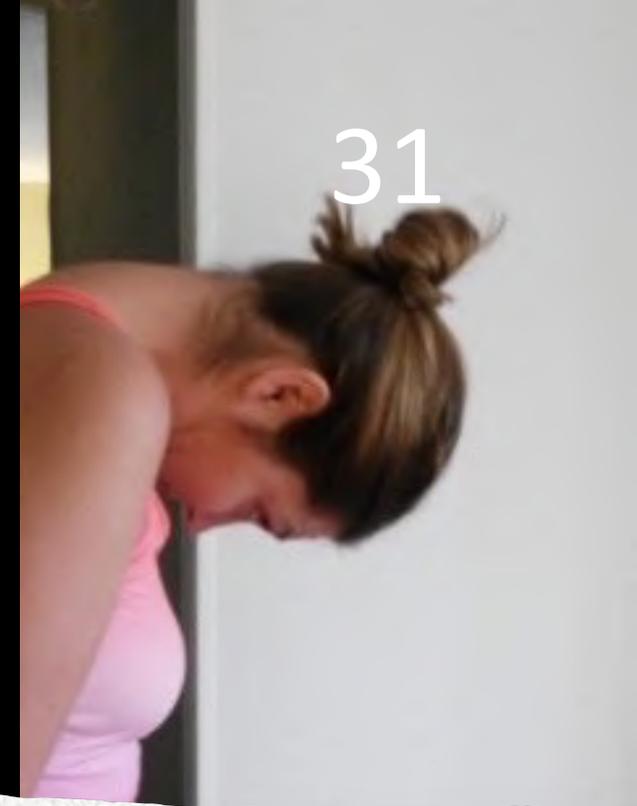
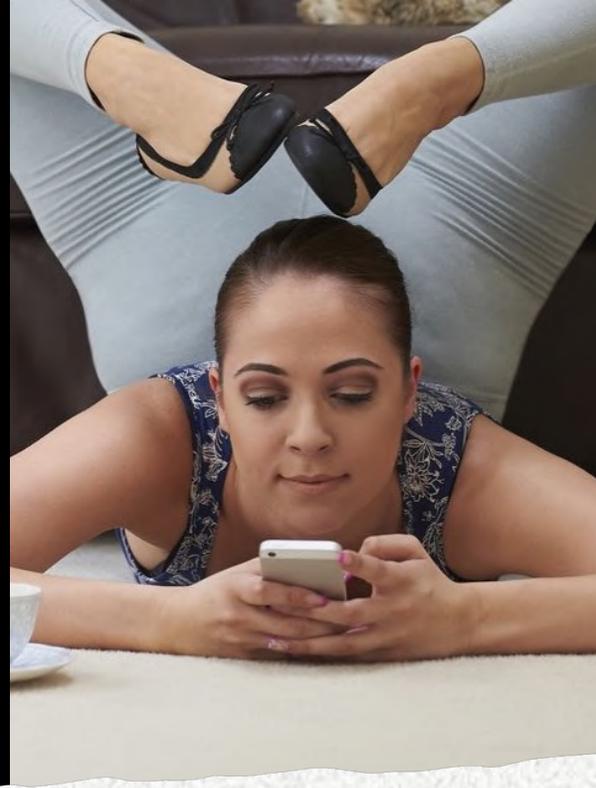


Hypermobility, Laxity, and Instability

- Many people with GJH do not experience problems
- Definitions:
 - **Hypermobility:** increased physiological motion
 - **Laxity:** excessive accessory motion
 - **Instability:** lack of motor control, perceived sense of the joint slipping out of place, inability to control motion at joints
- Being hypermobile is not necessarily a problem
 - Being unstable often is a problem
 - **Physical examination should focus on motor control, not just hypermobility**

(Nicholson, 2022b)





The Beighton Score does not measure all the important joints...

- The Beighton Score joints are only special for making an official diagnosis.
- Patients may be hypermobile in other joints, such as the shoulder, neck, lumbar spine, etc.
- Assess any joint that is problematic

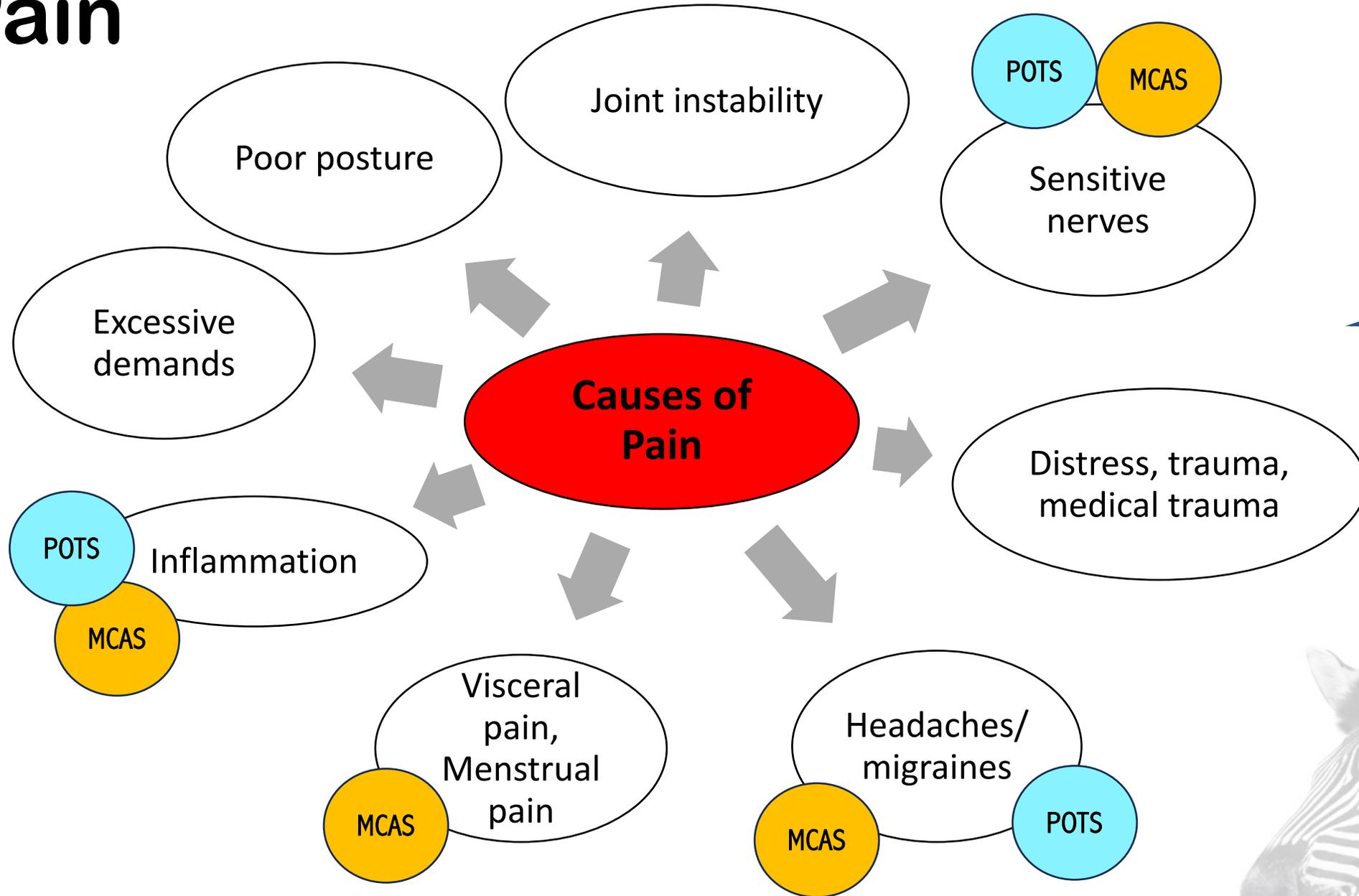
Pain Assessment

- Pain mechanism (guides best treatment):
 - Nociceptive: mechanical, inflammatory (thermal) – **“Issues with your Tissues”**
 - Peripheral or central neuropathic – **“Issues with your Tissues”**
 - Peripheral or central sensitization, nociplastic – **“Messed up volume control”**
- Source of pain (need to fix correct problems):
 - Muscles, joints, nerves, fascia, viscera, etc.
 - Psychosocial contributing factors, e.g., stress, anxiety, depression, etc.
- Perpetuating factors (so pain does not return):
 - Physical stressors to tissues
 - Factors causing local or systemic inflammation
 - Messed up volume control due to sensitization/nociplastic pain.

Daylor, 2023a;
Daylor, 2023b;
Chimente, 2018



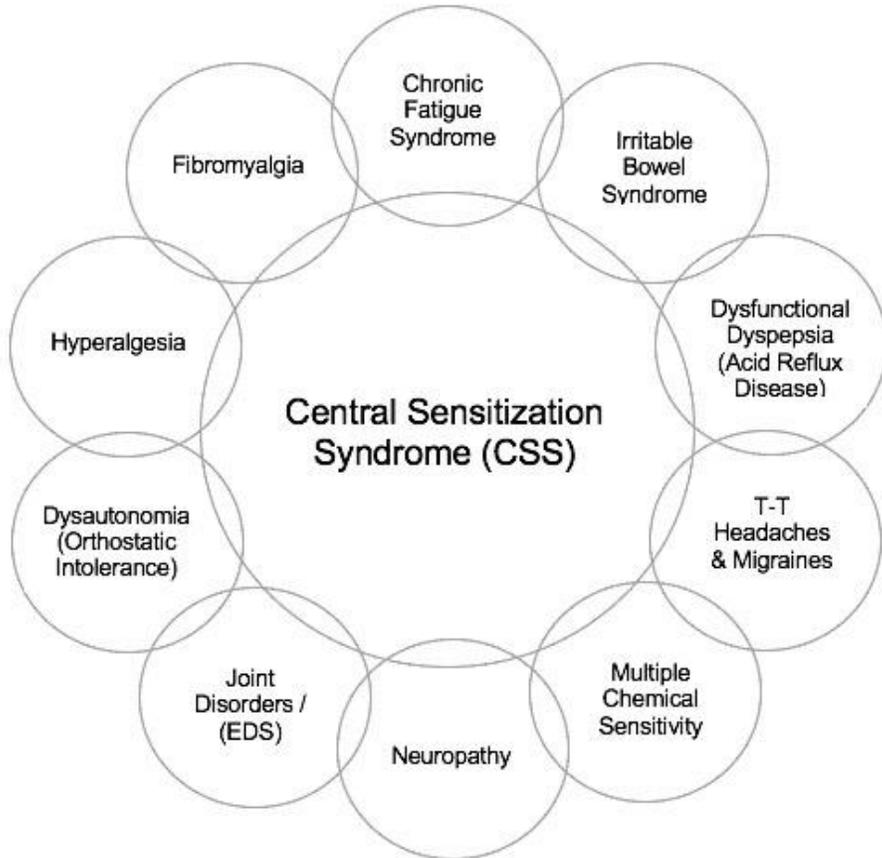
Pain



Several Pain Management Handouts



Pain Sensitivity



Central Sensitization Inventory	Never	Rarely	Some-times	Often	Always
1. Unrefreshed in the morning					
2. Muscles stiff/achy					
3. Pain all over the body					
4. Headaches					
5. Do not sleep well					
6. Difficulty concentrating					
7. Stress makes symptoms worse					
8. Tension in neck and shoulders					
9. Poor memory					
	0	1	2	3	4
Total score					

CSI-9 score

Subclinical 0-9

Mild 10-19

Mod/severe 20-36

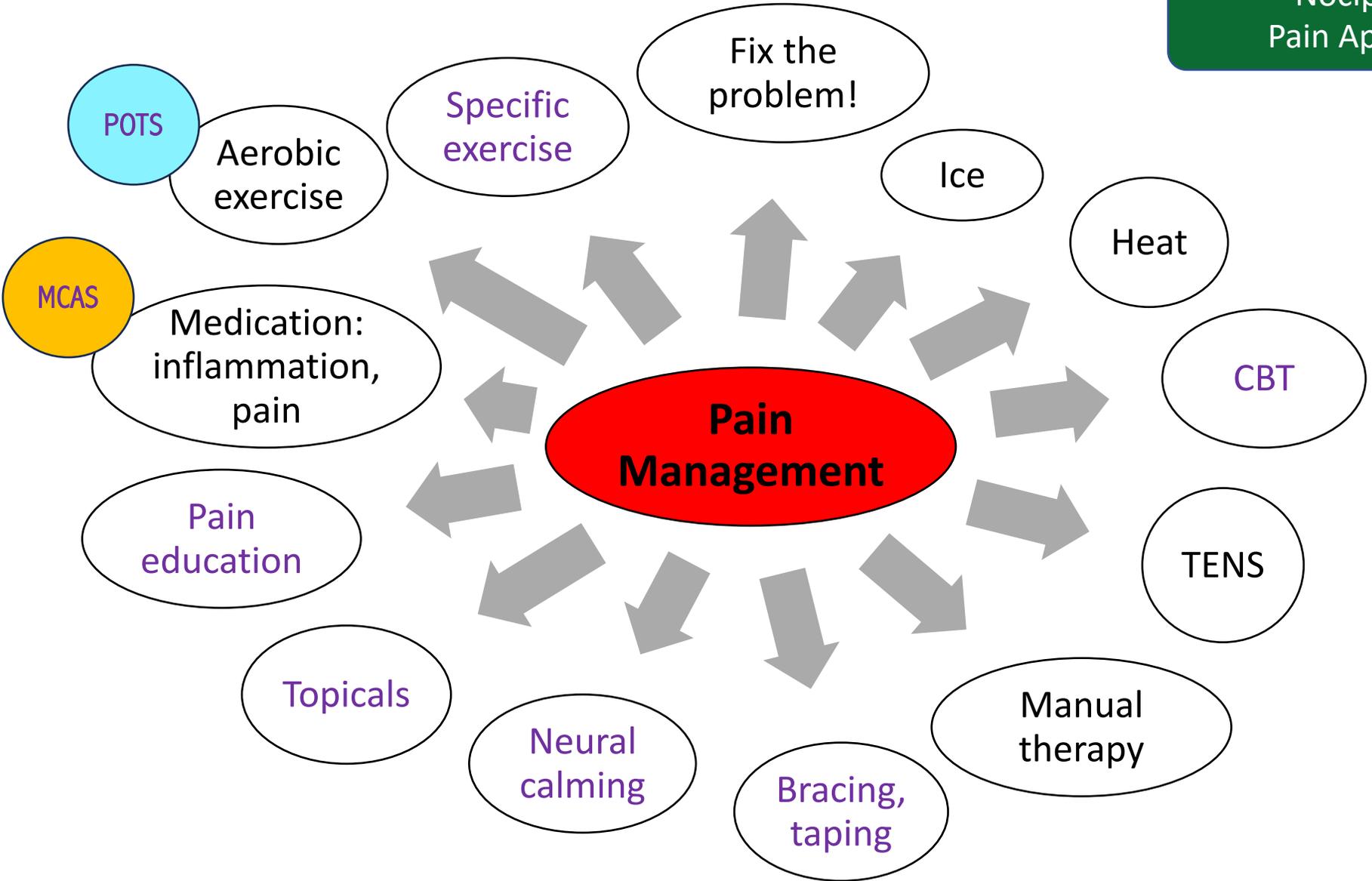
(Nishigami, 2018)

- Look for Central Sensitization and nociplastic pain
- Can measure with Central Sensitization Inventory-9

Nociplastic Pain

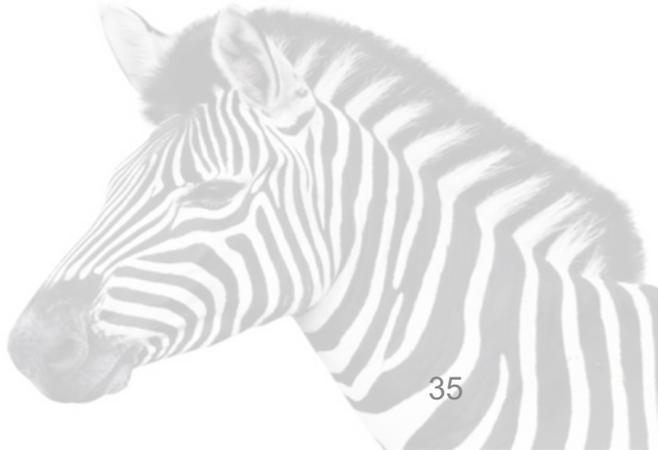


Nociplastic Pain
Pain Apps for Teens

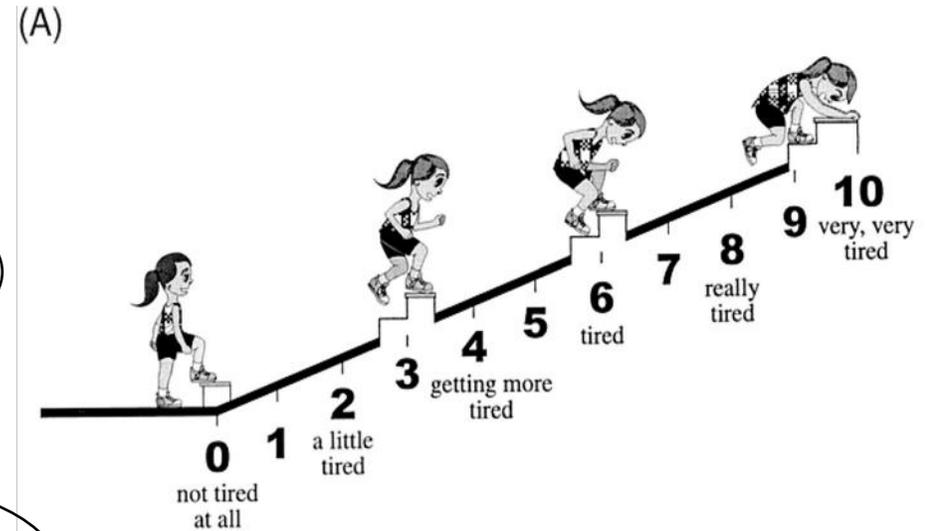
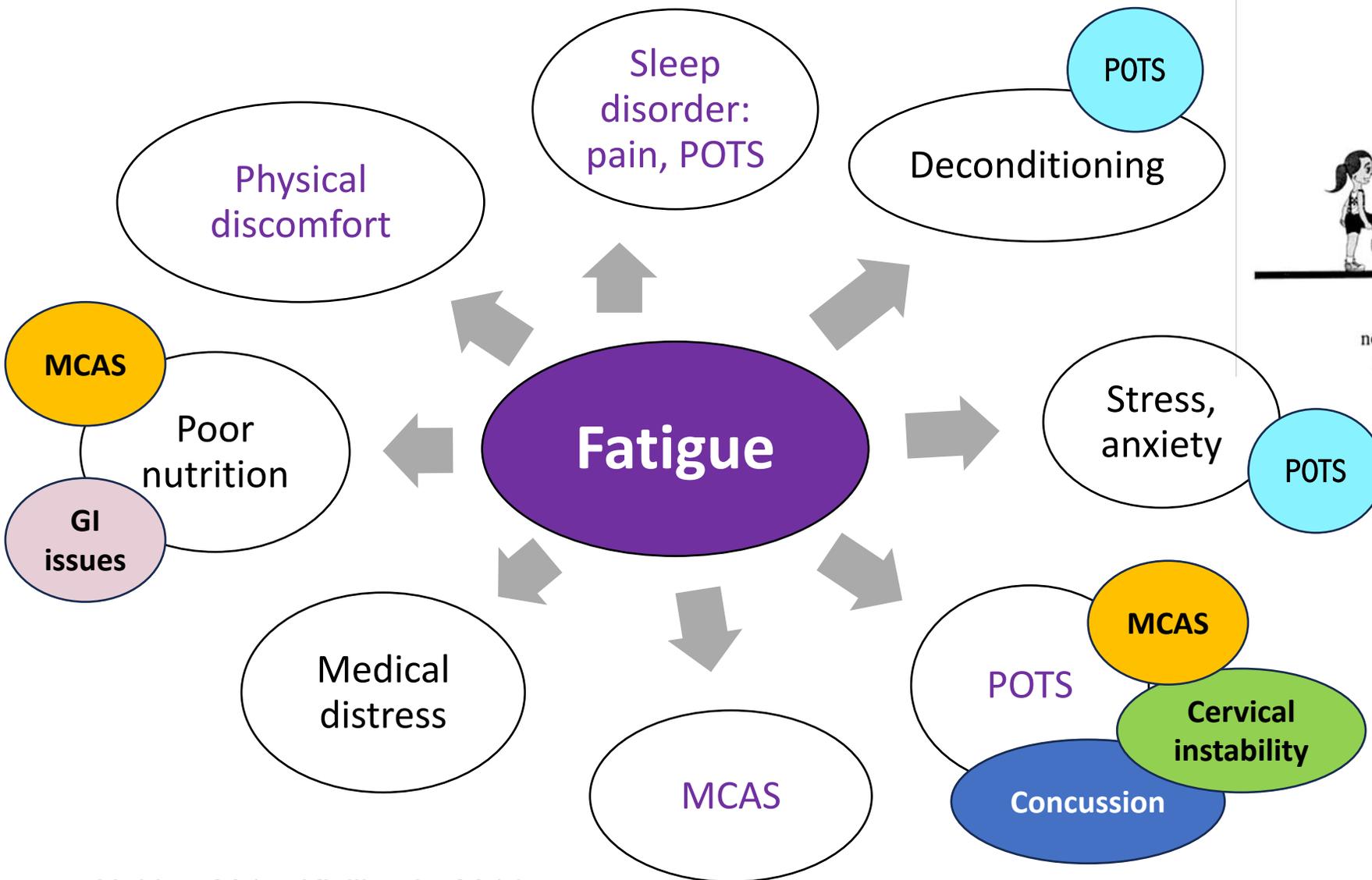


- Curable Pain CBT app (6 wks free)
- Free pain management apps for teens:
 - WebMAP
 - IBeatPain

I also have handouts available for items in **Purple text**



Fatigue/Sleep Problems



I have handouts available for items in **Purple text**



POTS NASA Stand/Lean Test

Easy to do in any clinic with pulse oximeter and BP cuff.
Takes 15 minutes

- Stand Test or Lean Test is as accurate as a Head-Up-Tilt-Table
- Supine 5 minutes, resting HR and BP, monitor symptoms
- Stand 10 min, leaning against a wall, no movement, fidgeting, talking
- Monitor HR, BP and symptoms at least at minute 1, 3, 5, 10
 - Recommended to repeat supine measurements after testing
- Positive test:
 - HR increase of >40 BPM in children and adolescents (>30 BPM for adult)
 - OR maximum HR >130 BPM, (6-12 y/o), 125 BPM (13-18 y/o)
 - Without BP drop: systolic > 20 mmHg or diastolic >10 mmHg
 - Monitor symptoms: dizziness, pre-syncope, cognitive changes, HA, hot flashes
 - Monitor hands and feet for changes in color
- May have negative test if pt is taking meds or using effective self-care

Seeley, 2023; Vernino, 2021; Chen, 2020; Bryarly, 2019

Test instructions/forms at <https://batemanhorncenter.org/wp-content/uploads/2016/09/NASA-LeanTest-Instructions-April-2018.pdf>



Physical Therapy Management of HSD/hEDS

Stratified Management of Hypermobility

SIMPLE/ EARLY

Episode of acute musculoskeletal injury, sprains, dislocation, subluxations, enthesopathies

SIMPLE/ EARLY

Ice, electrotherapy, tape, support, exercise (inc. proprioception & motor control), screen, educate; rehabilitate and prevent recurrence

INTERMEDIATE

Recurrent episodes, series of episodes at different sites, deconditioning, some central/peripheral sensitization, mild to moderate systemic conditions

INTERMEDIATE

Standard PT approaches have temporary effect, no effect or exacerbate. Need to address causative factors. More focus on functional restoration

COMPLEX/ LONG TERM

Chronic, longstanding, severe, unremitting pain with profound deconditioning, comorbidities, CNS involvement, and disability

COMPLEX/ LONG TERM

Multi-disciplinary management program using functional and cognitive behavioral approaches and assistive devices

PT Approach to Management of HSD

Assist patient in identifying and managing systemic comorbidities: education, treatment and/or referral

Decrease central, peripheral, and autonomic pain sensitization

Educate for correct posture and joint alignment, body mechanics, joint protection, appropriate use of splints and braces

Proprioceptive and motor control training, with training to relax muscles that are guarding

Stabilization, strengthening, muscle flexibility, aerobic conditioning

Integration of proper alignment & movement into function

Education about flare management

Patient Education

Educate and empower the patient/family

- Posture, joint protection, body mechanics, ergonomics
 - Orthotics, braces, & splints if/when needed
- Self-care, injury prevention, pain self-management
 - Problem-solving, braces, heat/ice, TENS, topicals, physiological quieting
- Appropriate exercise/activity
- Sleep hygiene & positioning; fatigue management, breathing
- POTS self-management and exercise progression
- Advice regarding impact of diet on POTS and MCAD
- Other issues: GI dysfunction, MCAD, incontinence, etc.
- Psychological & social wellness and coping

(Engelbert, 2017; Chopra, 2017; Russek, 2019; Simmonds, 2022)



Joint Protection and Posture



"the kids, with their heavy backpacks, head out to the bus" by [woodleywonderworks](#) is licensed under [CC BY 2.0](#).

- Choose appropriate postures, activities and exercises
- Provide proper support to the body
 - Good shoes, chairs, desks, pencils, etc.
- Adaptive tools, assistive devices, splints, braces, orthotics
- Teach patients not to hang on ligaments: e.g., not lock knees or hang on hips
- Avoid excessive forces, such as heavy lifting, high impact

(Engelbert, 2017; Revivo, 2019; Nicholson, 2022; Russek, 2019; Simmonds, 2022)



Pain Management Approach

1. Understand the pain: “Issues with the Tissues” vs. neuroplasticity
 - Type: nociceptive, neuropathic, nociplastic
 - Source: musculoskeletal tissues, CNS, viscera, psychosocial factors
 - Perpetuating factors: posture, body mechanics, guarding, psychological stress
2. Prevent pain from developing, when possible (e.g. posture)
3. Fix causes of pain, when possible (e.g., tight muscles, subluxed jts)
4. Calm nerves to ‘turn down the volume’ due to neuroplasticity
 - Use caution with pain management programs that ‘push through the pain’
5. Use strategies to manage pain (e.g., TENS, ice, topicals, etc.)
6. Optimize function (e.g., adapting the environment, braces, etc.)

The Debate About Bracing and Assistive Devices

- Braces, splints and assistive devices may be helpful intermittently to allow increased function (Nicholson, 2022)
- Supporting joints in ways that allow mobility and use may increase strength through increased functional activity (Callaghan, 2016; Azadinia, 2017)
- Immobilizing joints entirely may lead to weakness in the muscles controlling that joint
 - Patients should be committed to maintaining muscle strength when using immobilization braces



Orthotics, Braces, Splints

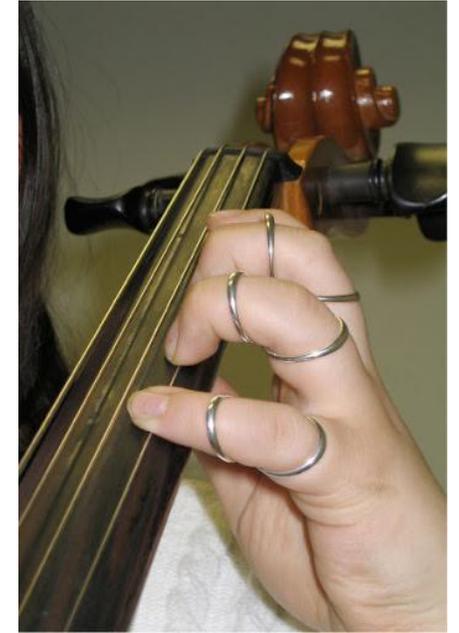


fb you know you have EDS when



Bauerfeind braces are popular among people with EDS:

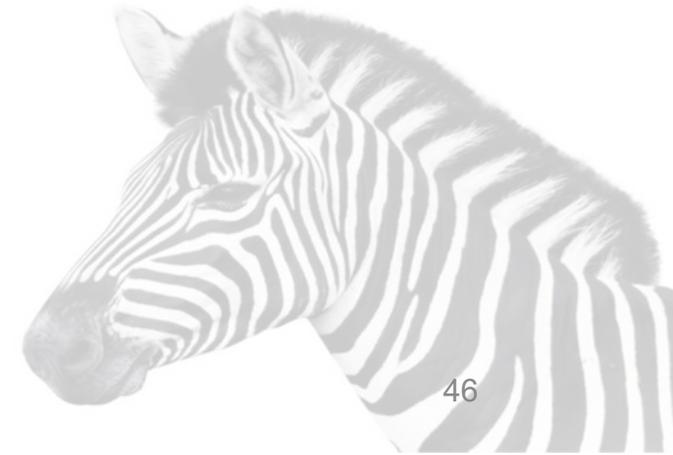
<https://www.bauerfeind.com/b2c/>



Silver Ring Splints are popular:
<https://www.silverringsplint.com>



Compression Garments (POTS or Proprio)

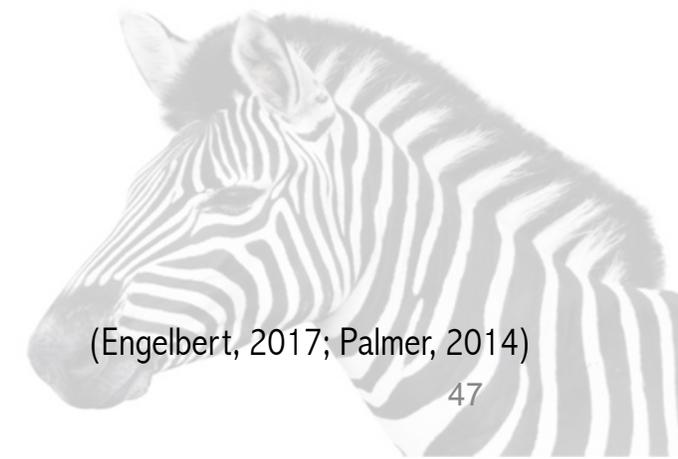


Thanks to Stephanie Carroll, RN, for suggesting these full body compression garments

- Bauerfeind makes many EDS-appropriate devices: <https://www.bauerfeind.com/b2c/>
- CWX makes sports compression garments: <https://cw-x.com>

Exercise Prescription

- Proprioception, stabilization, motor control & coordination
 - Start movements from good alignment
 - Make sure every movement is being done correctly, slowly with control
 - Teach pts to recognize and avoid excessive bracing and guarding
- Strengthening the correct muscles, relaxing muscles that should be relaxed
- Muscle endurance
- Appropriate muscle stretching, stabilizing surrounding joints
- Cardiovascular conditioning
- POTS-specific exercise
 - Horizontal positioning, pumping blood to the heart/head
 - ADaPT protocol (2023) or CHOP AADP Exercise Guide (2024)



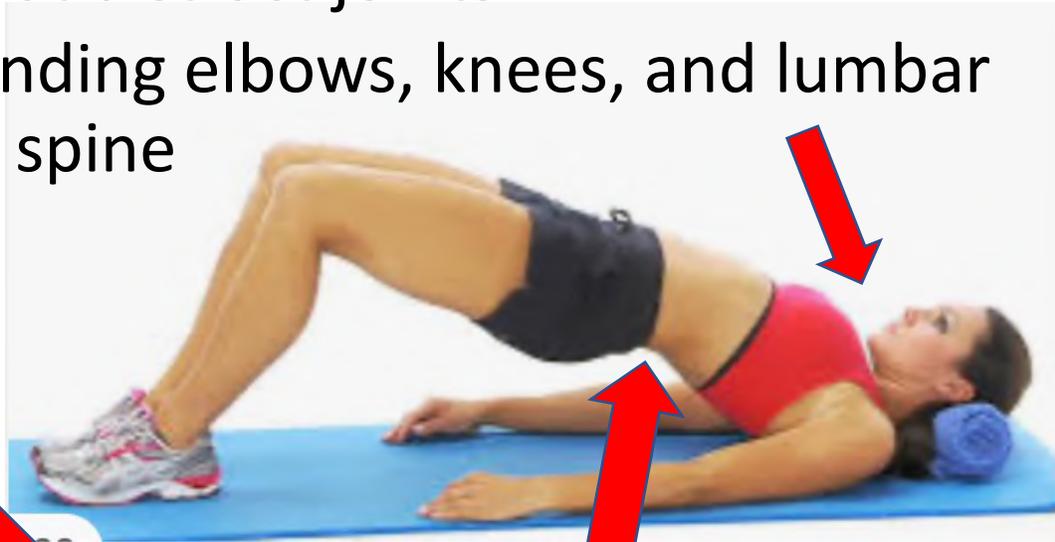
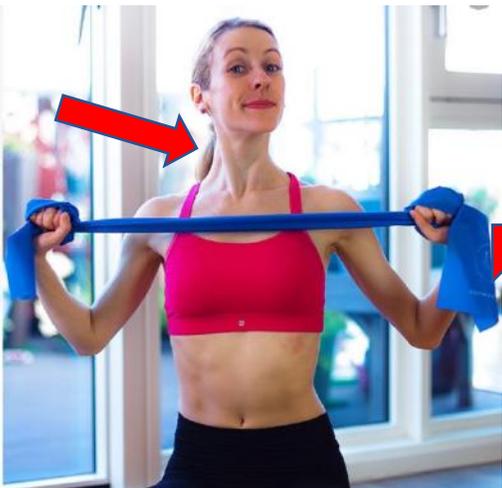
(Engelbert, 2017; Palmer, 2014)

Exercise: Do No Harm!

- Pts with HSD often have negative past experiences with PT due to:
 - Iatrogenic injuries from inappropriate exercise or manual therapy
 - Unmet rehabilitation needs (Bovet, 2016; Simmonds, 2019)
- Avoid mechanical pain due to excessive tissue stress
 - With poor proprioception & motor control, patients do exercises incorrectly
 - Tissues often start weaker than in deconditioned non-HSD patients
 - Tensile strength changes with activity, age, inflammatory state, menses
 - Slow progression to allow for slower histological changes: “Start low, go slow”
- Pay attention to other joints, nerves, excessive tension, posture, orthostatic position

Don't Stress Other Joints!

- Be careful with:
 - Gripping weights or resistance bands
 - Weight on extended wrists
 - Weights that distract joints
 - Hyperextending elbows, knees, and lumbar or cervical spine



Proprioception, Motor Control, Stabilization Training

- Emphasize proprioception and motor control before strengthening
- Improve joint alignment, exercise in optimal alignment
- Strengthen deep stabilizing muscles around joints
 - Strengthen first in physiological range, then in hypermobile range
- Elongate tight muscles while stabilizing joints
- Both generalized fitness and patient-specific exercises help
- Start low, go slow!
- Exercises must be appropriate, not be too difficult, pts must be able to do them correctly, must have time & equipment

(Nicholson, 2022; Kemp, 2010; Birt, 2014)



Evidence for Benefits of Exercise

- Exercise can decrease pain, improve function, decrease kinesiophobia and disability (Zibriskie, 2022; van Meulenbroek, 2020)
- Some studies of exercise show that generalized fitness is as effective as HSD-specific exercises in reducing pain and improving function (Feldman, 2020; Kemp, 2010)
- Exercise in neutral and exercise progressing into hypermobile ranges can both be beneficial (Pacey, 2013)
- Optimal mode, intensity, and progression for HSD are not yet known (Zabriskie, 2022)
- Exercise can also address POTS fatigue and pain (Junghans-Rutelonis, 2019)

Reasons Why Past Exercise May Have Failed

- Failing to treat the whole person, other HSD/POTS/MCAS issues
- Failing to address proprioceptive and motor control deficits before strengthening or aerobic conditioning
- Using exercises that are too aggressive:
 - Using what works for other pts, not accounting for deconditioning, fragile connective tissue
- Not continuing exercises for long enough:
 - 4-6 weeks might not be enough, people with HSD/EDS tend to start weaker and progress slowly
- Performing exercises too often:
 - Too intense can cause flares. Maybe 1x/week better than 2-3x/wk
- Patient is too overwhelmed or affected by other symptoms to even do exercises

(Simmonds 2019; Scheper, 2013; Birt, 2014; Engelbert, 2006)



Manual Therapy: **Do No Harm!**

- Gentle soft tissue manual therapy is often appropriate and helpful
- Very light/controlled joint mobilization may be appropriate and helpful – e.g., Mobilization with Movement, muscle energy techniques
- But...
 - Do not over-mobilize!
 - Do not manipulate unless you really understand HSD and know what you are doing
- Treat cautiously, as you would a pregnant or post-partum patient
- If the patient gets worse every time you touch them – work on central sensitization



Medical Management of HSD



Multidisciplinary Management

- Van Meulenbroek (2020) implemented multidisciplinary program:
 - Cognitive behavioral approaches
 - Fear avoidance education/management
 - Exercise (proprioception, core stability, strength, aerobic and hydrotherapy) with home exercise program
 - Education of parents
- Multidisciplinary management focused on improving function also significantly decreased pain
- Comprehensive, multidisciplinary pain management (PT, OT, counseling, relaxation training, medication) can decrease pain and improve function in HSD
- Patient/family education benefits both children and parents

(Revivo, 2019)

(Revivo, 2019; Nicholson, 2022)

Medications

- Little definitive research evidence for medications
- Limit NSAIDs to use for true inflammation
 - NSAIDs may slow tissue healing, aggravate GI & MCAS symptoms
- Tricyclics, anti-seizure, SNRI meds for neuropathic pain
- Topical analgesics and anti-inflammatory medications
- Acetaminophen
- Low dose naltrexone (LDN) seems to be helpful (Daylor, 2023b)
 - It is a mast cell stabilizer in the brain
- Cautions:
 - Opiates for short term use only
 - Muscle relaxers and Botox may aggravate instability



Surgical Precautions

- Orthopedic surgery (e.g. rotator cuff or ACL repair) is only effective 34% of the time in patients with hEDS; this is 50% as often as non-hypermobile pts. Therefore, it is important that conservative management (with an hEDS knowledgeable provider) be fully explored before resorting to surgery.
- Orthopedic surgeries in hEDS are more likely to have complications, with one study reporting 91% complication rate.
- Surgeons should take hEDS into account when planning surgery.
- Spinal surgery complications rate is higher in HSD/hEDS than in the general population.
- Gastrointestinal surgeries in hEDS are more likely to have complications, but fewer complications than vascular EDS. Typical complications include arterial perforation or tears, bowel perforation or tears, recurrent hernias or increased bleeding.

Rombaut, 2011; Yonko, 2021; Homere, 2020; Chi, 2023; Kulas Sjøborg, 2017; Burcharth, 2012)

Surgical and Anesthetic Precautions:
Hypermobility Spectrum Disorder (HSD) and
Hypermobile Ehlers Danlos Syndrome (hEDS)

The main feature of HSD/hEDS is *laxity of connective tissue*, including skin, ligaments, blood vessels and nerves. This can cause *potentially fatal problems* for these patients when unconscious, and/or having surgery.

BEWARE THE UNCONSCIOUS PATIENT!	<i>In the unconscious HSD/hEDS patient, a little force may displace any joint.</i> Treat unconscious HSD/hEDS patients with full spinal stabilization as if they have a spinal injury. If you don't, then you may cause one! Use NO traction on limbs. Use extreme care with the chest: the ribs easily dislocate front or back.
BEWARE THE LARYNGOSCOPE!	Use extreme gentleness, with minimal, if any, anterior traction on the laryngoscope. The jaw may dislocate on one or both sides. Manipulation of the laryngoscope can also damage the cricopharyngeal muscle and its nerves, the esophagus and the cervical spine.
BEWARE NECK MOTION!	Keep patient's head in neutral position throughout. Movement of unstable subcranial joints may cause spinal cord damage during incautious patient handling during anesthesia. Consider a soft collar.
LOCAL ANESTHESIA	HSD/hEDS patients are often resistant to local anesthetics: they may need much larger doses than other patients, and these may need to be repeated during a procedure. Ropivacaine may work better than lidocaine or bupivacaine.
SURGICAL TECHNIQUE	Use minimal force when cutting or moving tissues. Cut blood vessels may contract poorly: electrocautery is appropriate. Tissue healing may be prolonged. Close layers without tension using slowly-absorbable or non-absorbable sutures. Reinforce them with steri-strips etc. as appropriate.
BLEEDING & BRUISING	These are due to fragile small blood vessels, not an intrinsic blood disorder, so elaborate clotting tests are rarely indicated. Be alert for slowly-accumulating, deep hematomas.
POST-OPERATIVE PAIN	Painful polyneuropathy is common in HSD/hEDS. Post-operative pain may be more severe and more prolonged than normal. Be liberal with analgesics.
CARDIO-VASCULAR INSTABILITY	HSD/hEDS patients are subject to hypotension and/or tachycardia due to low blood volume, and defective venoconstriction. Liberal IV fluids usually can address this.
GI DYSFUNCTION	Poor GI motility is routine in HSD/hEDS, worse after surgery. Minimize constipating agents, and use laxatives pre-emptively. Consider pro-motility agents.
CARDIAC RESCUCITATION	Some HSD/hEDS patients have loose costosternal joints , sometimes palpably displaced. For them, chest compressions could in theory be very dangerous, causing rib detachments, a flail chest and even heart or lung puncture by freed anterior ribs. There is no consensus on whether cardiac resuscitation should include chest compressions in patients with clear evidence of rib displacements.

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This document is online at www.AlanSpanosMD.com. It was updated March 2019.

For more information, see the Ehlers Danlos Society at ehlers-danlos.com.

Handout for patients to share with surgeons and anesthesiologists

This handout and many others to share with your health care providers by Dr. Spanos, MD (retired)
<https://rachelleepac.com/spanos-resources/>

Also my Surgical Precautions handout



What Can YOU do for These Patients?

- Recognize hypermobility and consider whether it contributes to their problems
- Believe the patient, validate their experience
- Help them “connect the dots” with signs & symptoms other than musculoskeletal – especially POTS and MCAS. Making sense of their various S&S can help a lot, psychologically.
- Help them find knowledgeable providers: PT, OT, GI, neurologists, allergists/immunologists, hematologists, psychologists, etc...
- Provide safe treatment – medications, prescriptions for splints, referrals, etc.
- Discourage treatments that might be harmful: some medications, surgeries, excessive diagnostic testing...
- **You ARE seeing these patients with HSD/hEDS – even if they are not diagnosed**

Alan Hakim, Rheumatologist, EDS Specialist, London

When to Refer to Specialist for Dx

Table 1. Indications for further investigation or non-general practitioner specialist referral in the presence of joint hypermobility

Patient	Patient's history	Family history
<ul style="list-style-type: none"> • Blue sclera • Tall or short stature • Cardiac murmurs • Skin fragility • Lens dislocation • High myopia • Ectopic lentis • Developmental disability • Intellectual disability • Dysmorphic features • Cleft palate/bifid uvula • Multiple congenital anomalies • Marfanoid body habitus 	<ul style="list-style-type: none"> • Cardiac valve disease • Congenital heart disease • Vascular rupture or dissection • Low-force fractures (two in children) • Talipes equinovarus • Severe scoliosis • Wide atrophic scars • Poor wound healing • Aortic dilatation on echocardiography • Recurrent hernia • Organ rupture • Recurrent pneumothoracies 	<ul style="list-style-type: none"> • Cardiac valve disease • Congenital heart disease • Vascular rupture or dissection • Mitral valve prolapse • Sudden unexplained death • Low-force fractures (three in adults) • Formally diagnosed early onset osteoporosis • Aortic dilatation on echocardiography • Organ rupture • Recurrent pneumothoracies

Nicholson, 2022;

There is limited benefit to referring for genetic testing unless you suspect something OTHER than HSD



Summary

- Look for HSD when things don't make sense
 - ***“When you can't connect the issues, think connective tissues”***
- HSD impairments may affect all systems in the body, not just joints
- Physical therapy is key to helping patients manage pain, fatigue, musculoskeletal & functional aspects of HSD
 - People with HSD don't always tolerate 'standard' PT. PT should never make things worse!
- Each patient with HSD is an individual – there is no standard Rx for everyone.
- This is a chronic condition and patients may benefit from extended or recurrent care
- LISTEN to patients and BELIEVE what they say!
 - Medical traumatization is real (Halverson, 2023)



Handouts Available

- <https://webpace.clarkson.edu/~lrussek/research.html>
- General Information
 - [Overview of Hypermobility Spectrum Disorder](#)
 - [HSD in children and adolescents](#)
 - [Checklist of physical therapy treatment approaches for HSD/hEDS.](#)
 - [Surgical precautions for people with HSD/hEDS.](#)
 - [List of HSD and POTS disability/accommodations resources.](#)
- Self-Care Strategies
- Pain Management
- Exercise
- Managing POTS and MCAS



Available on my website



Hypermobility Lecture Series Schedule

- HSD 101: Basics of HSD/hEDS and self-care
- HSD 102: POTS and POTS self-care, basics of MCAS
- HSD 103: Pain management in HSD/hEDS
- HSD 104: Safe exercise selection and progression with HSD/hEDS
- HSD 105: Posture and joint protection
- HSD 106: Gut issues in HSD/hEDS, POTS, MCAS
- HSD 107: Fatigue in HSD/hEDS and POTS
- HSD 108: Headaches, migraines, & TMJ pain associated with HSD, POTS and MCAS
- HSD 109: Breathing disorders in HSD
- HSD 110: Lumbar instability
- HSD 111: Conservative management of cervical instability
- HSD 112: The vagus nerve
- HSD 113: The role of fascia
- HSD 114: Hospitalization and surgery with HSD, POTS, MCAD

I will refer to these if you want more info



Resources for Hypermobility

- [The Ehlers-Danlos Society](#), Has many excellent resources for all forms of EDS. It also has a list of EDS healthcare providers, and support groups in the US. Based in the US.
 - Conferences and on-line workshops: <https://www.ehlers-danlos.com/upcoming-events/>
 - On-line training programs: <https://www.ehlers-danlos.com/echo/>
- [The Ehlers-Danlos Syndrome Toolkit](#). Information about diagnosis, management and available resources intended for primary care and other health providers.
- ["Hypermobility Syndromes" booklet for patients](#). 27 pages discussing all aspects of hypermobility.
- [Hypermobility Syndromes Association \(HMSA\)](#).
- [NASEM Report on HSD/EDS and disability](#). The National Academy of Science, Engineering and Medicine report that I helped create is a comprehensive overview of functional limitations that may lead to disability people with HSD/EDS. It also lists many potential accommodations.
- [School Toolkit for HSD/EDS](#). Great ideas to help kids succeed in school. Lots of printable handouts to bring to school to facilitate communication and understanding
- ***Taming the Zebra***, book by P. Stott and H. Purdin, about systemic issues in HSD/hEDS.

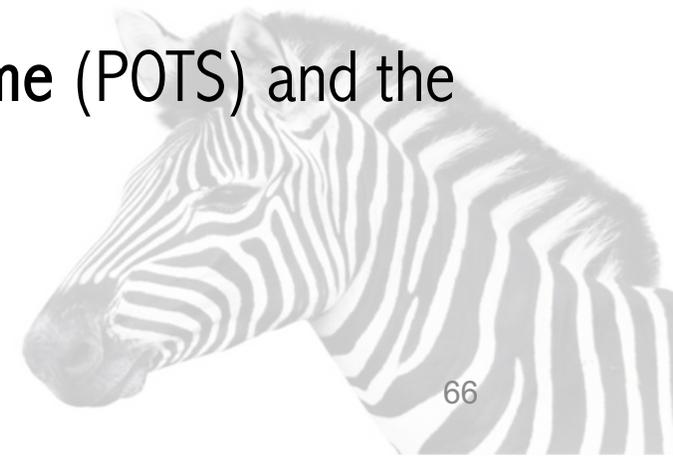
Resources for POTS

- **Good primary care overview:** Seeley MC, Lau DH, Gallagher C. Postural Orthostatic Tachycardia Syndrome: Diagnosis and Management Guide for Nurses. *Nursing: Research and Reviews*. 2023;13:41-49.
- **Thorough review:** Vernino S, Bourne KM, Stiles LE, et al. Postural orthostatic tachycardia syndrome (POTS): State of the science and clinical care from a 2019 National Institutes of Health Expert Consensus Meeting - Part 1. *Auton Neurosci*. Nov 2021;235:102828.
- **Dysautonomia International** has great patient info: <http://www.dysautonomiainternational.org>
- **NASA Lean Test instructions:** <https://batemanhornecenter.org/wp-content/uploads/2016/09/NASA-Lean-Test-Instructions-1.pdf>



Resources for GI Problems

- Lam C, Amarasinghe G, Zarate-Lopez N, Fikree A, Byrne P, Kiani-Alikhan S, et al. Gastrointestinal symptoms and nutritional issues in patients with **hypermobility** disorders: assessment, diagnosis and management. *Frontline Gastroenterol.* 2023;14(1):68-77.
 - <https://fg.bmj.com/content/flgastro/14/1/68.full.pdf>
- Weinstock LB, Pace LA, Rezaie A, Afrin LB, Molderings GJ. **Mast Cell Activation Syndrome: A Primer for the Gastroenterologist.** *Dig Dis Sci.* 2021;66(4):965-82.
 - <https://link.springer.com/article/10.1007/s10620-020-06264-9>
- DiBaise JK, Harris LA, Goodman B. **Postural Tachycardia Syndrome (POTS) and the GI Tract: A Primer for the Gastroenterologist.** *Am J Gastroenterol.* 2018;113(10):1458-67.



Resources for MCAS

- Afrin LB, Butterfield JH, Raithel M, Molderings GJ. Often seen, rarely recognized: mast cell activation disease--a guide to diagnosis and therapeutic options. *Ann Med*. 2016;48(3):190-201. *Good overview*.
- Afrin L, Molderings GJ. A concise, practical guide to diagnostic assessment for mast cell activation disease. *World J Hematol*. 2014;3(1):1-17. *Includes validated questionnaire to identify MCAS signs and symptoms*
- Information for both patients and health care providers:
 - <https://www.tmsforacure.org>
 - <https://www.mastzellaktivierung.info/en/introduction.html>
- Summary for health care providers: https://tmsforacure.org/wp-content/uploads/Mast_Cell_Disease_Primer_Slides_TMS_09.20.2021_Final.pdf
- Medication recommendations, starting with OTC H1 and H2 inhibitors
 - <https://tmsforacure.org/treatments/medications-treat-mast-cell-diseases/>

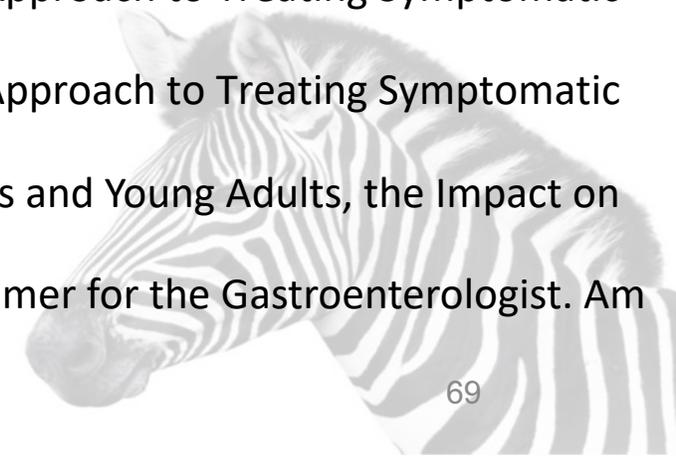


References 1

- Adib N, Davies K, Grahame R, Woo P, Murray KJ. Joint hypermobility syndrome in childhood. A not so benign multisystem disorder? *Rheumatology (Oxford)*. 2005;44(6):744-50.
- Afrin L, Molderings GJ. A concise, practical guide to diagnostic assessment for mast cell activation disease. *World J Hematol*. 2014;3(1):1-17.
- Afrin LB, Butterfield JH, Raithel M, Molderings GJ. Often seen, rarely recognized: mast cell activation disease--a guide to diagnosis and therapeutic options. *Ann Med*. 2016;48(3):190-201.
- Aubry-Rozier B, Schwitzguebel A, Valerio F, et al. Are patients with hypermobile Ehlers–Danlos syndrome or hypermobility spectrum disorder so different? *Rheumatology international*. 2021;41(10):1785-1794.
- Azadinia F, Ebrahimi ET, Kamyab M, Parnianpour M, Cholewicki J, Maroufi N. Can lumbosacral orthoses cause trunk muscle weakness? A systematic review of literature. *Spine J*. 2017;17(4):589-602.
- Birt L, Pfeil M, Macgregor A, Armon K, Poland F. Adherence to home physiotherapy treatment in children and young people with joint hypermobility: a qualitative report of family perspectives on acceptability and efficacy. *Musculoskeletal Care*. 2014;12(1):56-61.
- Blajwajs L, Williams J, Timmons W, Sproule J. Hypermobility prevalence, measurements, and outcomes in childhood, adolescence, and emerging adulthood: a systematic review. *Rheumatol Int*. Aug 2023;43(8):1423-1444.
- Boris JR, Bernadzikowski T. Prevalence of joint hypermobility syndromes in pediatric postural orthostatic tachycardia syndrome. *Auton Neurosci*. Mar 2021;231:102770.
- Boris JR, McClain ZBR, Bernadzikowski T. Clinical Course of Transgender Adolescents with Complicated Postural Orthostatic Tachycardia Syndrome Undergoing Hormonal Therapy in Gender Transition: A Case Series. *Transgend Health*. 2019;4(1):331-334.
- Bryarly M, Phillips LT, Fu Q, Vernino S, Levine BD. Postural Orthostatic Tachycardia Syndrome: JACC Focus Seminar. *J Am Coll Cardiol*. Mar 19 2019;73(10):1207-1228.
- Bulbena A, Rosado S, Cabaleiro M, et al. Validation of the neuroconnective endophenotype questionnaire (NEQ): a new clinical tool for medicine and psychiatry resulting from the contribution of Ehlers-Danlos syndrome. *Front Med (Lausanne)*. 2023;10:1039223.
- Bulbena-Cabré A, Baeza-Velasco C, Rosado-Figuerola S, Bulbena A. Updates on the psychological and psychiatric aspects of the Ehlers-Danlos syndromes and hypermobility spectrum disorders. *Am J Med Genet C Semin Med Genet*. Dec 2021;187(4):482-490.
- Burcharth J, Rosenberg J. Gastrointestinal surgery and related complications in patients with Ehlers-Danlos syndrome: a systematic review. *Dig Surg*. 2012;29(4):349-57.

References 2

- Callaghan MJ, Parkes MJ, Felson DT. The Effect of Knee Braces on Quadriceps Strength and Inhibition in Subjects With Patellofemoral Osteoarthritis. *J Orthop Sports Phys Ther.* 2016;46(1):19-25.
- Castori M, Tinkle B, Levy H, Grahame R, Malfait F, Hakim A. A framework for the classification of joint hypermobility and related conditions. *Am J Med Genet C Semin Med Genet.* 2017;175(1):148-57.
- Chen G, Du J, Jin H, Huang Y. Postural Tachycardia Syndrome in Children and Adolescents: Pathophysiology and Clinical Management. *Front Pediatr.* 2020;8:474.
- Chi J, Raso J, Tadepalli V, et al. Outcomes Following Anterior Cervical Discectomy and Fusion in Patients With Ehlers-Danlos Syndrome. *Global Spine J.* Jan 16 2023:21925682231151924.
- Chimenti RL, Frey-Law LA, Sluka KA. A Mechanism-Based Approach to Physical Therapist Management of Pain. *Phys Ther.* May 1 2018;98(5):302-314.
- Chopra P, Tinkle B, Hamonet C, et al. Pain management in the Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet.* Mar 2017;175(1):212-219.
- Copetti M, Morlino S, Colombi M, Grammatico P, Fontana A, Castori M. Severity classes in adults with hypermobile Ehlers–Danlos syndrome/hypermobility spectrum disorders: a pilot study of 105 Italian patients. *Rheumatology.* 2019;58(10):1722-1730.
- Daylor V, Gensemer C, Norris RA, Bluestein L. Hope for Hypermobility: Part 1—An Integrative Approach to Treating Symptomatic Joint Hypermobility. *Topics in Pain Management.* 2023;38(8):1-9.
- Daylor V, Gensemer C, Norris RA, Bluestein L. Hope for Hypermobility: Part 2—An Integrative Approach to Treating Symptomatic Joint Hypermobility. *Topics in Pain Management.* 2023;38(9):1-11.
- de Vries J, Verbunt J, Stubbe J, et al. Generalized Joint Hypermobility and Anxiety in Adolescents and Young Adults, the Impact on Physical and Psychosocial Functioning. *Healthcare (Basel).* Apr 29 2021;9(5).
- DiBaise JK, Harris LA, Goodman B. Postural Tachycardia Syndrome (POTS) and the GI Tract: A Primer for the Gastroenterologist. *Am J Gastroenterol.* 2018;113(10):1458-67.

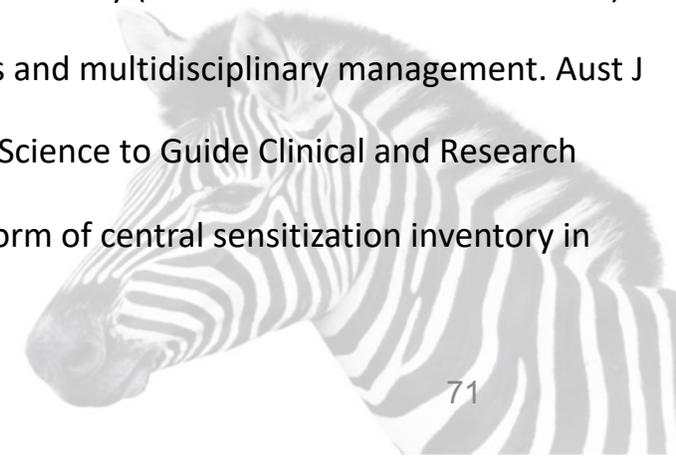


References 3

- Eccles JA, Quadt L, McCarthy H, et al. Variant connective tissue (joint hypermobility) and its relevance to depression and anxiety in adolescents: a cohort-based case-control study. *BMJ Open*. Nov 30 2022;12(12):e066130.
- Engelbert RH, van Bergen M, Henneken T, Helders PJ, Takken T. Exercise tolerance in children and adolescents with musculoskeletal pain in joint hypermobility and joint hypomobility syndrome. *Pediatrics*. 2006;118(3):e690-6.
- Engelbert RHH, Juul-Kristensen B, Pacey V, De Wandele I, Smeenk S, Woinarosky N, et al. The Evidence-based rationale for physical therapy treatment of children, adolescents and adults diagnosed with joint hypermobility syndrome/hypermobile Ehlers Danlos Syndrome. *Am J Med Genet C Semin Med Genet*. 2017;175(1):158-67.
- Feldman ECH, Hivick DP, Slepian PM, Tran ST, Chopra P, Greenley RN. Pain Symptomatology and Management in Pediatric Ehlers-Danlos Syndrome: A Review. *Children (Basel)*. 2020;7(9).
- Hakim A, De Wandele I, O'Callaghan C, Pocinki A, Rowe P. Chronic fatigue in Ehlers-Danlos syndrome-Hypermobility type. *Am J Med Genet C Semin Med Genet*. Mar 2017;175(1):175-180.
- Hakim A, O'Callaghan C, De Wandele I, Stiles L, Pocinki A, Rowe P. Cardiovascular autonomic dysfunction in Ehlers-Danlos syndrome-Hypermobility type. *Am J Med Genet C Semin Med Genet*. Mar 2017;175(1):168-174.
- Halverson CME, Penwell HL, Francomano CA. Clinician-associated traumatization from difficult medical encounters: Results from a qualitative interview study on the Ehlers-Danlos Syndromes. *SSM - Qualitative Research in Health*. 2023/06/01/ 2023;3:100237.
- Henderson FC, Sr., Austin C, Benzel E, et al. Neurological and spinal manifestations of the Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet*. Mar 2017;175(1):195-211.
- Homere A, Bolia IK, Juhan T, Weber AE, Hatch GF. Surgical Management of Shoulder and Knee Instability in Patients with Ehlers-Danlos Syndrome: Joint Hypermobility Syndrome. *Clin Orthop Surg*. Sep 2020;12(3):279-285.
- Jones JT, Black WR, Moser CN, Rush ET, Malloy Walton L. Gender dysphoria in adolescents with Ehlers-Danlos syndrome. *SAGE Open Med*. 2022;10:20503121221146074.
- Junghans-Rutelonis AN, Postier A, Warmuth A, Schwantes S, Weiss KE. Pain Management In Pediatric Patients With Postural Orthostatic Tachycardia Syndrome: Current Insights. *J Pain Res*. 2019;12:2969-80.

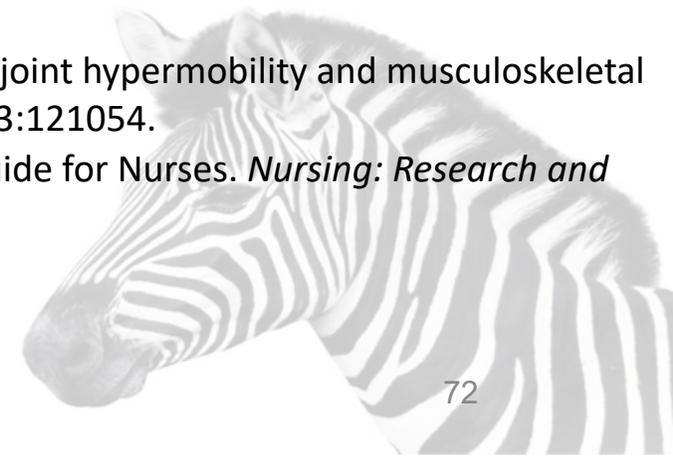
References 4

- Kalisch L, Hamonet C, Bourdon C, Montalescot L, de Cazotte C, Baeza-Velasco C. Predictors of pain and mobility disability in the hypermobile Ehlers-Danlos syndrome. *Disabil Rehabil.* 2019;1-8.
- Kemp S, Roberts I, Gamble C, et al. A randomized comparative trial of generalized vs targeted physiotherapy in the management of childhood hypermobility. *Rheumatology (Oxford).* Feb 2010;49(2):315-25.
- Kindgren E, Quiñones Perez A, Knez R. Prevalence of ADHD and Autism Spectrum Disorder in Children with Hypermobility Spectrum Disorders or Hypermobile Ehlers-Danlos Syndrome: A Retrospective Study. *Neuropsychiatr Dis Treat.* 2021;17:379-88.
- Kizilbash SJ, Ahrens SP, Bruce BK, et al. Adolescent fatigue, POTS, and recovery: a guide for clinicians. *Curr Probl Pediatr Adolesc Health Care.* 2014;44(5):108-133.
- Kulas Sjøborg ML, Leganger J, Rosenberg J, Burcharth J. Increased Need for Gastrointestinal Surgery and Increased Risk of Surgery-Related Complications in Patients with Ehlers-Danlos Syndrome: A Systematic Review. *Dig Surg.* 2017;34(2):161-170.
- Kumskova M, Flora GD, Staber J, Lentz SR, Chauhan AK. Characterization of bleeding symptoms in Ehlers-Danlos syndrome. *J Thromb Haemost.* Jul 2023;21(7):1824-1830.
- Lam C, Amarasinghe G, Zarate-Lopez N, et al. Gastrointestinal symptoms and nutritional issues in patients with hypermobility disorders: assessment, diagnosis and management. *Frontline Gastroenterol.* 2023;14(1):68-77.
- Malfait F, Francomano C, Byers P, et al. The 2017 international classification of the Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet.* Mar 2017;175(1):8-26.
- Molderings GJ, Haenisch B, Bogdanow M, Fimmers R, Nothen MM. Familial occurrence of systemic mast cell activation disease. *PLoS One.* 2013;8(9):e76241.
- National Academies of Sciences Engineering and Medicine. Selected Heritable Disorders of Connective Tissue and Disability (The National Academies Press.) (2022).
- Nicholson LL, Chan C, Tofts L, Pacey V. Hypermobility syndromes in children and adolescents: Assessment, diagnosis and multidisciplinary management. *Aust J Gen Pract.* 2022a;51(6):409-14.
- Nicholson LL, Simmonds J, Pacey V, et al. International Perspectives on Joint Hypermobility: A Synthesis of Current Science to Guide Clinical and Research Directions. *J Clin Rheumatol.* Sep 1 2022b;28(6):314-320.
- Nishigami T, Tanaka K, Mibu A, Manfuku M, Yono S, Tanabe A. Development and psychometric properties of short form of central sensitization inventory in participants with musculoskeletal pain: A cross-sectional study. *PLoS One.* 2018;13(7):e0200152.



References 5

- Pacey V, Tofts L, Adams RD, Munns CF, Nicholson LL. Exercise in children with joint hypermobility syndrome and knee pain: a randomised controlled trial comparing exercise into hypermobile versus neutral knee extension. *Pediatr Rheumatol Online J*. 2013;11(1):30.
- Palmer S, Bailey S, Barker L, Barney L, Elliott A. The effectiveness of therapeutic exercise for joint hypermobility syndrome: a systematic review. *Physiotherapy*. Sep 2014;100(3):220-7.
- Peterson B, Coda A, Pacey V, Hawke F. Physical and mechanical therapies for lower limb symptoms in children with Hypermobility Spectrum Disorder and Hypermobile Ehlers-Danlos Syndrome: a systematic review. *J Foot Ankle Res*. 2018;11:59.
- Revivo G, Amstutz DK, Gagnon CM, McCormick ZL. Interdisciplinary Pain Management Improves Pain and Function in Pediatric Patients with Chronic Pain Associated with Joint Hypermobility Syndrome. *PM&R*. Feb 2019;11(2):150-157.
- Rombaut L, Malfait F, De Wandele I, et al. Medication, surgery, and physiotherapy among patients with the hypermobility type of Ehlers-Danlos syndrome. *Arch Phys Med Rehabil*. Jul 2011;92(7):1106-12.
- Rugg-Gunn FJ. Non-epileptic paroxysmal neurological and cardiac events: the differential diagnosis of epilepsy. 2009;
- Russek LN, Block NP, Byrne E, et al. Presentation and physical therapy management of upper cervical instability in patients with symptomatic generalized joint hypermobility: International expert consensus recommendations. *Front Med (Lausanne)*. 2022;9:1072764.
- Russek LN, Stott P, Simmonds J. Recognizing and Effectively Managing Hypermobility-Related Conditions. *Phys Ther*. Sep 1 2019;99(9):1189-1200.
- Russek LN. Is it really fibromyalgia? Recognizing mast cell activation, orthostatic tachycardia, and hypermobility. *Orthopaedic Practice*. 2018;30(3):187-193.
- Scheper MC, Engelbert RH, Rameckers EA, Verbunt J, Remvig L, Juul-Kristensen B. Children with generalised joint hypermobility and musculoskeletal complaints: state of the art on diagnostics, clinical characteristics, and treatment. *Biomed Res Int*. 2013;2013:121054.
- Seeley MC, Lau DH, Gallagher C. Postural Orthostatic Tachycardia Syndrome: Diagnosis and Management Guide for Nurses. *Nursing: Research and Reviews*. 2023;13:41-49.



References 6

- Seneviratne SL, Maitland A, Afrin L. Mast cell disorders in Ehlers-Danlos syndrome. *Am J Med Genet C Semin Med Genet*. Mar 2017;175(1):226-236.
- Simmonds JV, Herbland A, Hakim A, Ninis N, Lever W, Aziz Q, et al. Exercise beliefs and behaviours of individuals with Joint Hypermobility syndrome/Ehlers-Danlos syndrome - hypermobility type. *Disabil Rehabil*. 2019;41(4):445-55.
- Simmonds JV. 2022. Masterclass: Hypermobility and hypermobility related disorders. *Musculoskelet Sci Pract*. 57:102465. 10.1016/j.msksp.2021.102465
- Tinkle B, Castori M, Berglund B, et al. Hypermobile Ehlers–Danlos syndrome (aka Ehlers–Danlos syndrome Type III and Ehlers–Danlos syndrome hypermobility type): Clinical description and natural history. *Wiley Online Library*; 2017:48-69.
- To M, Simmonds J, Alexander C. Where do People with Joint Hypermobility Syndrome Present in Secondary Care? The Prevalence in a General Hospital and the Challenges of Classification. *Musculoskeletal Care*. Mar 2017;15(1):3-9.
- Tofts, L. J., Simmonds, J., Schwartz, S. B., Richeimer, R. M., O'Connor, C., Elias, E., ... & Pacey, V. (2023). Pediatric joint hypermobility: a diagnostic framework and narrative review. *Orphanet journal of rare diseases*, 18(1), 1-10.
- Van Meulenbroek T, Conijn AEA, Huijnen IPJ, Engelbert RHH, Verbunt JA. Multidisciplinary Treatment for Hypermobile Adolescents with Chronic Musculoskeletal Pain. *J Rehabil Med Clin Commun*. 2020;3:1000033.
- Vernino S, Bourne KM, Stiles LE, et al. Postural orthostatic tachycardia syndrome (POTS): State of the science and clinical care from a 2019 National Institutes of Health Expert Consensus Meeting - Part 1. *Auton Neurosci*. Nov 2021;235:102828.
- Weinstock LB, Pace LA, Rezaie A, Afrin LB, Molderings GJ. Mast Cell Activation Syndrome: A Primer for the Gastroenterologist. *Dig Dis Sci*. 2021;66(4):965-82.
- Yonko EA, LoTurco HM, Carter EM, Raggio CL. Orthopedic considerations and surgical outcomes in Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet*. Dec 2021;187(4):458-465.
- Zabriskie HA. Rationale and Feasibility of Resistance Training in hEDS/HSD: A Narrative Review. *J Funct Morphol Kinesiol*. 2022;7(3).
- Zhang Q, Xu B, Du J. Update of Individualized Treatment Strategies for Postural Orthostatic Tachycardia Syndrome in Children. *Front Neurol*. 2020;11:525.

Thank
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Questions?

