An Introduction to 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
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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
   - Recognize presentation of common comorbidities: Postural Orthostatic Tachycardia Syndrome (POTS) and Mast Cell Activation Syndrome (MCAS)
2. List potential medical problem areas in these patients
3. Describe a management approach to Hypermobile Spectrum Disorders
4. Access useful resources for managing these patients

Patient handouts on my website
https://webspace.clarkson.edu/~lrussek/research.html

Why the Zebra?

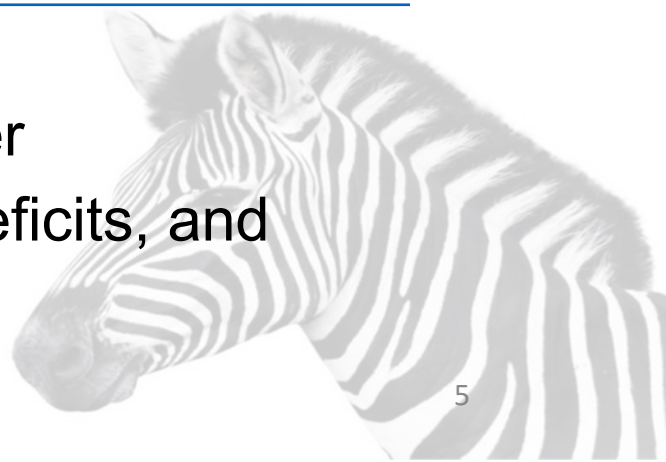
- Most health professionals have learned: “When you hear hoofbeats, look for horses, not zebras.”
- But people with HSD *are* different, and they need to be treated differently.
- Treating a zebra as though it were a horse does not work well.
- “Why Zebras are not Horses” information sheet for PTs: https://webspace.clarkson.edu/~lrussek/docs/hypermobility/Zebras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

https://www.postery.com/us/zebra-poster-2

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)



PRIMEVIEW

THE EHLERS–DANLOS SYNDROMES

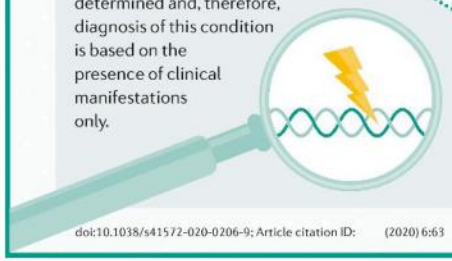
nature reviews disease primers

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).

DIAGNOSIS

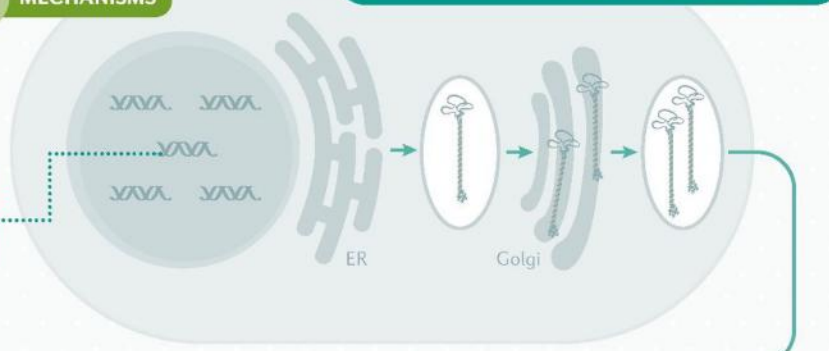
The symptoms of EDS are diverse and differ between subtypes. Symptoms that are found in multiple EDS subtypes include joint hypermobility, soft and hyperextensible skin, poor wound healing, pain and easy bruising. Vascular and musculoskeletal symptoms are present in some subtypes. Diagnostic work-up 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.

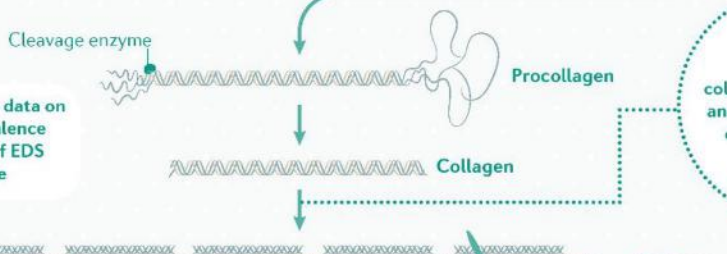


MECHANISMS

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

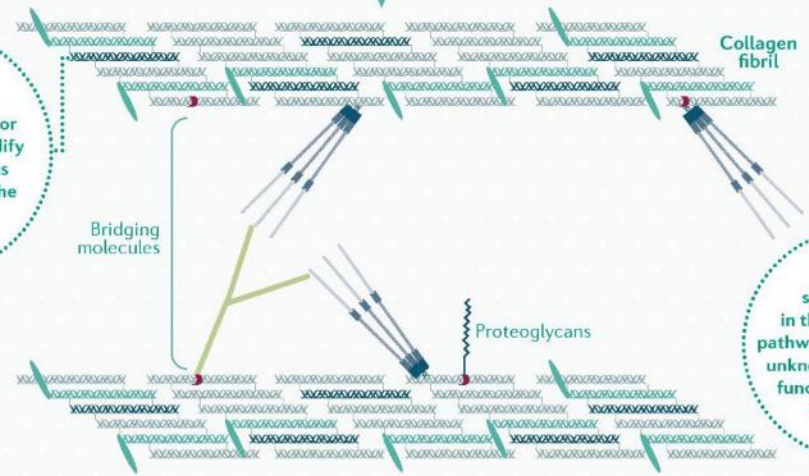
Variants in genes encoding the fibrillar procollagens I, III and V, or in genes encoding enzymes responsible for cleaving procollagen to mature collagen, lead to collagen fibrils with an abnormal structure or composition





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

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



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

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

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.

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.

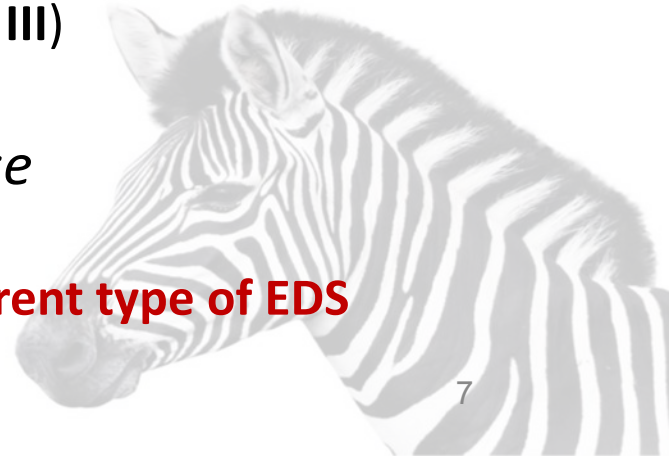
doi:10.1038/s41572-020-0206-9; Article citation ID: (2020) 6:63

Written by Louise Adams; designed by Laura Marshall

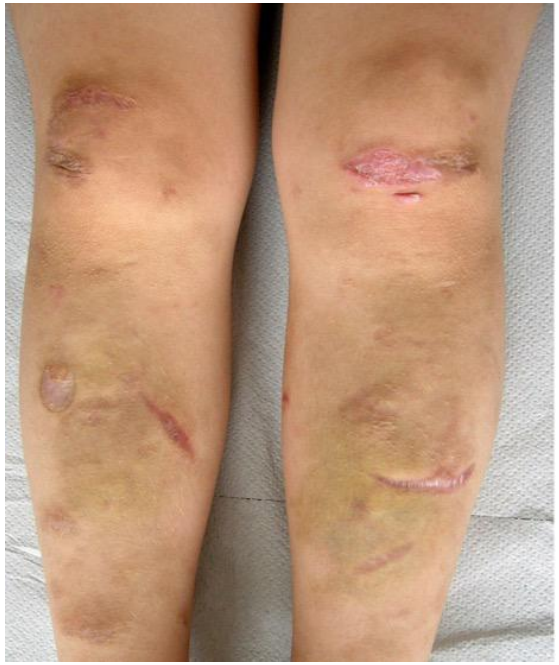
Pathophysiology (for reference)

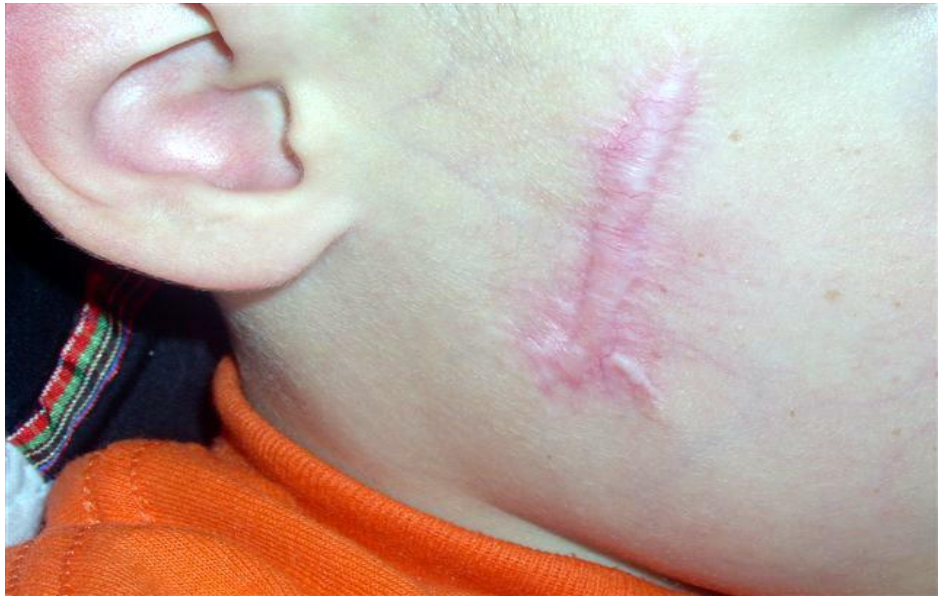
Types of EDS and Hypermobility

- 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**

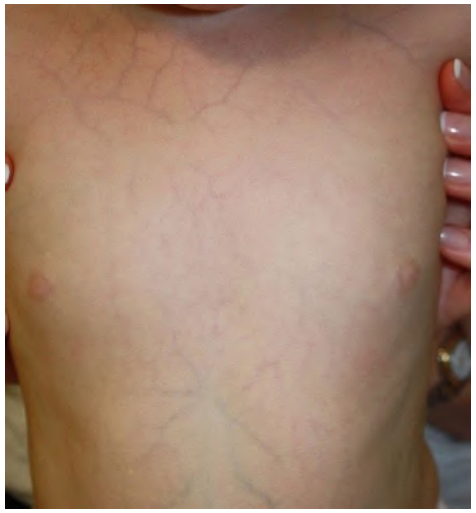


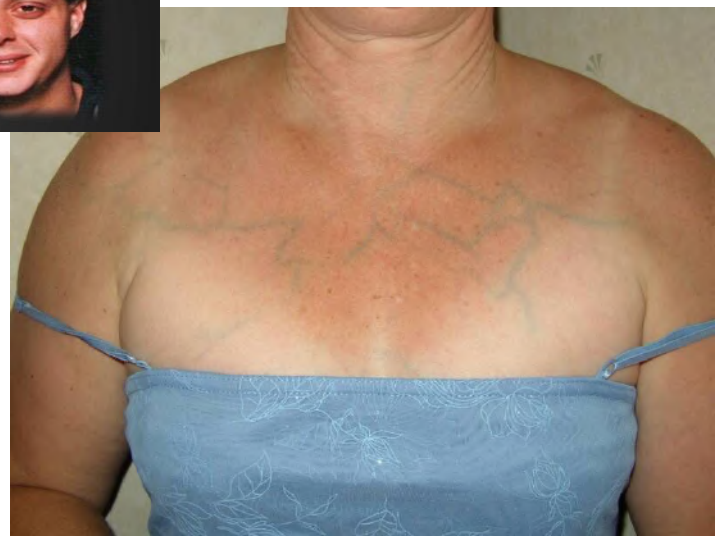
Classical EDS





Vascular EDS





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

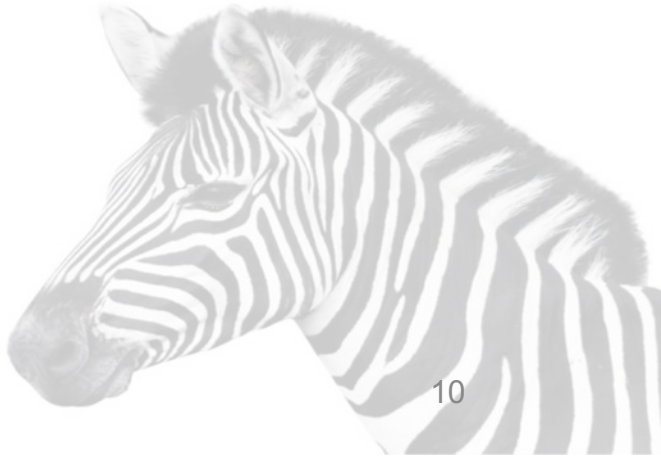
**Note, these signs may be present in hEDS, usually less dramatic*

www.ehlersdanlosnetwork.org/vascular.html
https://www.pinterest.cl/pin/558868634993169756/
https://www.annabelleschallenge.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

The Ehlers Danlos Society

A. 5th FINGER / 'PINKIES'

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

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

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

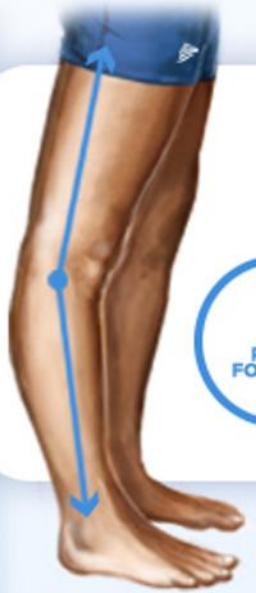
1 POINT FOR EACH HAND

B. THUMBS

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

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

1 POINT FOR EACH THUMB



1 POINT FOR EACH LEG

D. KNEES

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

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

C. ELBOWS

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

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

1 POINT FOR EACH ARM

E. SPINE

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

If yes, **add one point.**

1 POINT

Used with permission from the Ehlers-Danlos Society, https://www.ehlers-danlos.com/assessing-joint-hypermobility/

Diagnosis: Adults 2017 hEDS Criteria

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

hEDS Must meet <u>all 3 criteria</u>:

1. Generalized joint hypermobility
2. Two of the following:
   - A. ≥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**

The International Consortium on Ehlers-Danlos Syndromes & Related Disorders
In Association with The Ehlers-Danlos Society

Diagnostic Criteria for Hypermobile Ehlers-Danlos Syndrome (hEDS)

This diagnostic checklist is for doctors across all disciplines to be able to diagnose EDS

Distributed by The Ehlers Danlos Society.

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

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

CRITERION 1 – Generalized Joint Hypermobility

One of the following selected:

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

Beighton Score: ____/9

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

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

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

Feature A (five must be present)

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

Feature A total: ____/12

Feature B

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

Feature C (must have at least one)

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

CRITERION 3 – All of the following prerequisites MUST be met

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

Diagnosis: _____

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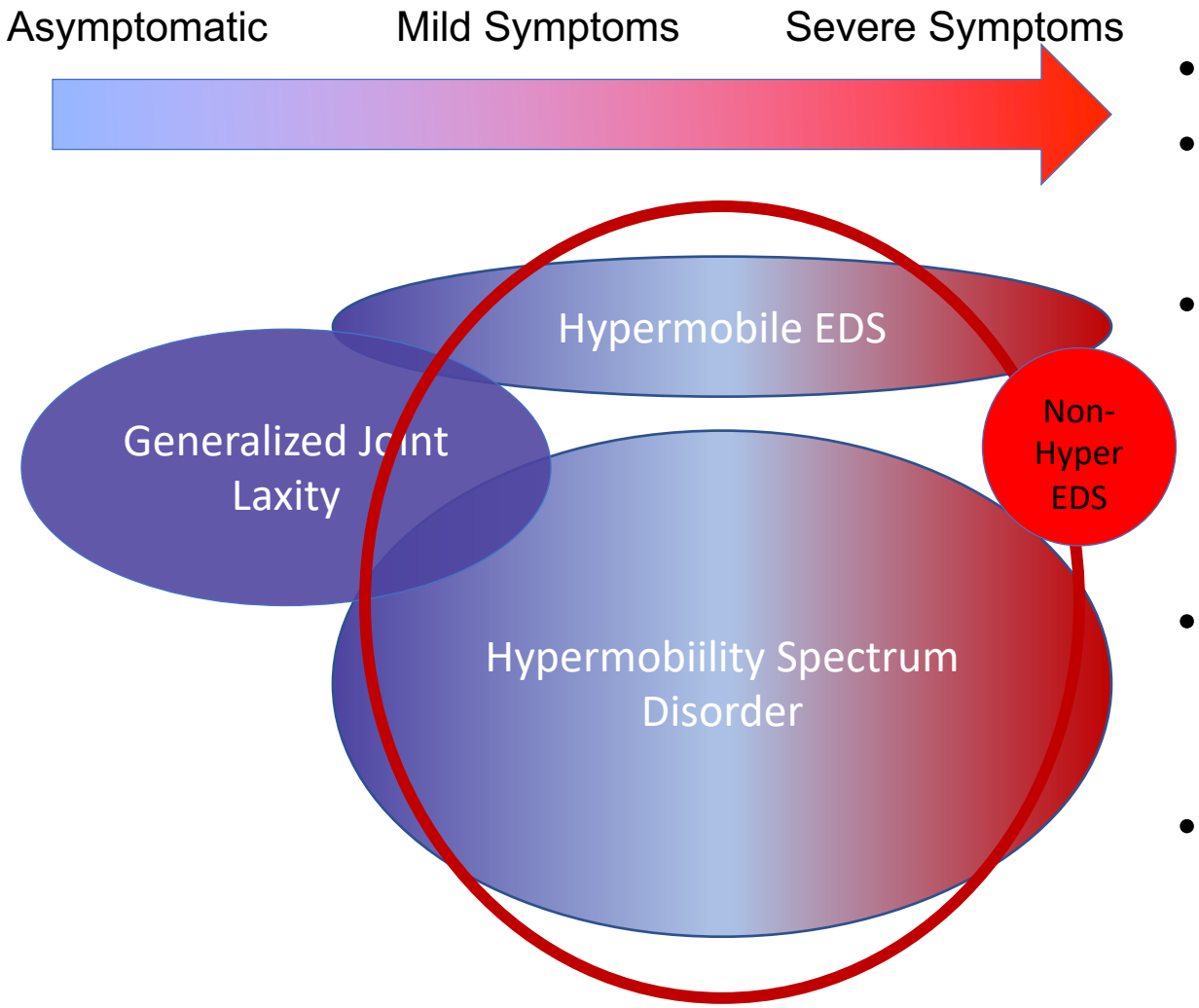
Diagnostic checklist in handout and at https://www.ehlers-danlos.com/heds-diagnostic-checklist/

HSD vs. hEDS



- 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 generally 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.

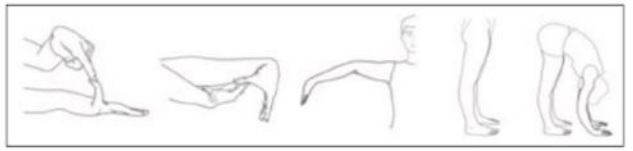
2023 Joint Hypermobility Criteria for Children

Five key questions to ask:

1. Generalized joint hypermobility
   a. Beighton Score ≥ 6
2. Skin and Tissue Abnormalities
   a. 3 out of 6 criteria → skin involvement subtype
3. Musculoskeletal complications
   a. 2 out of 3 criteria → HSD
4. Co-morbidities
   a. Yes → 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

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- ☐ 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

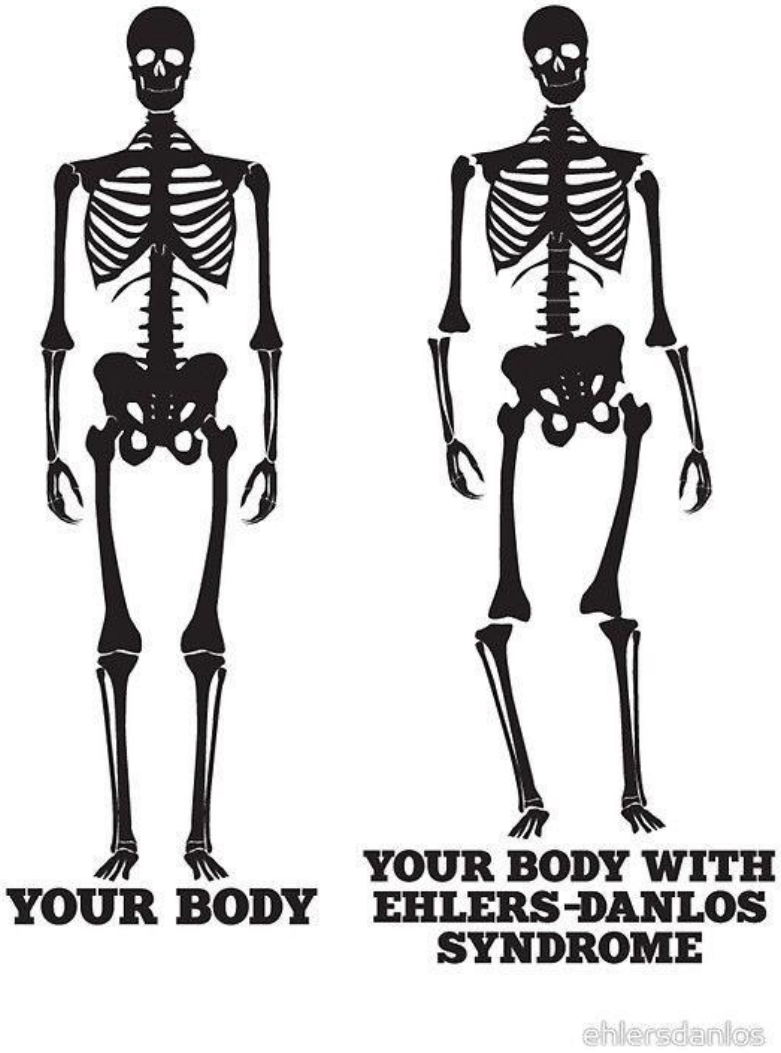
Co-Morbidities

- ☐ 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”



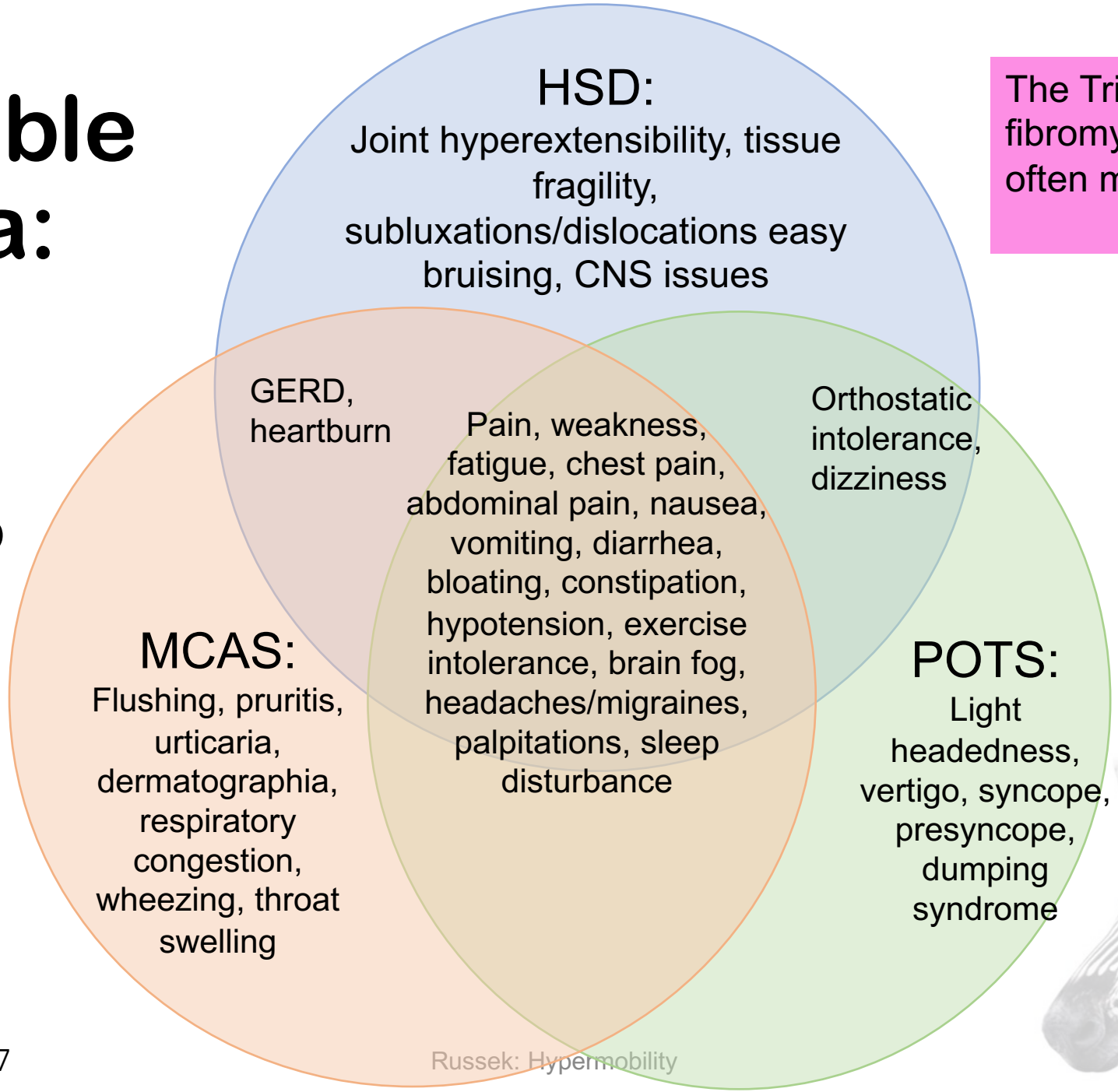
Presentation & Comorbidities

Overview of HSD

- **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, cervico-medullary 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

Russek, 2019; Simmons, 2022

The Terrible Trifecta: HSD POTS MCAS



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

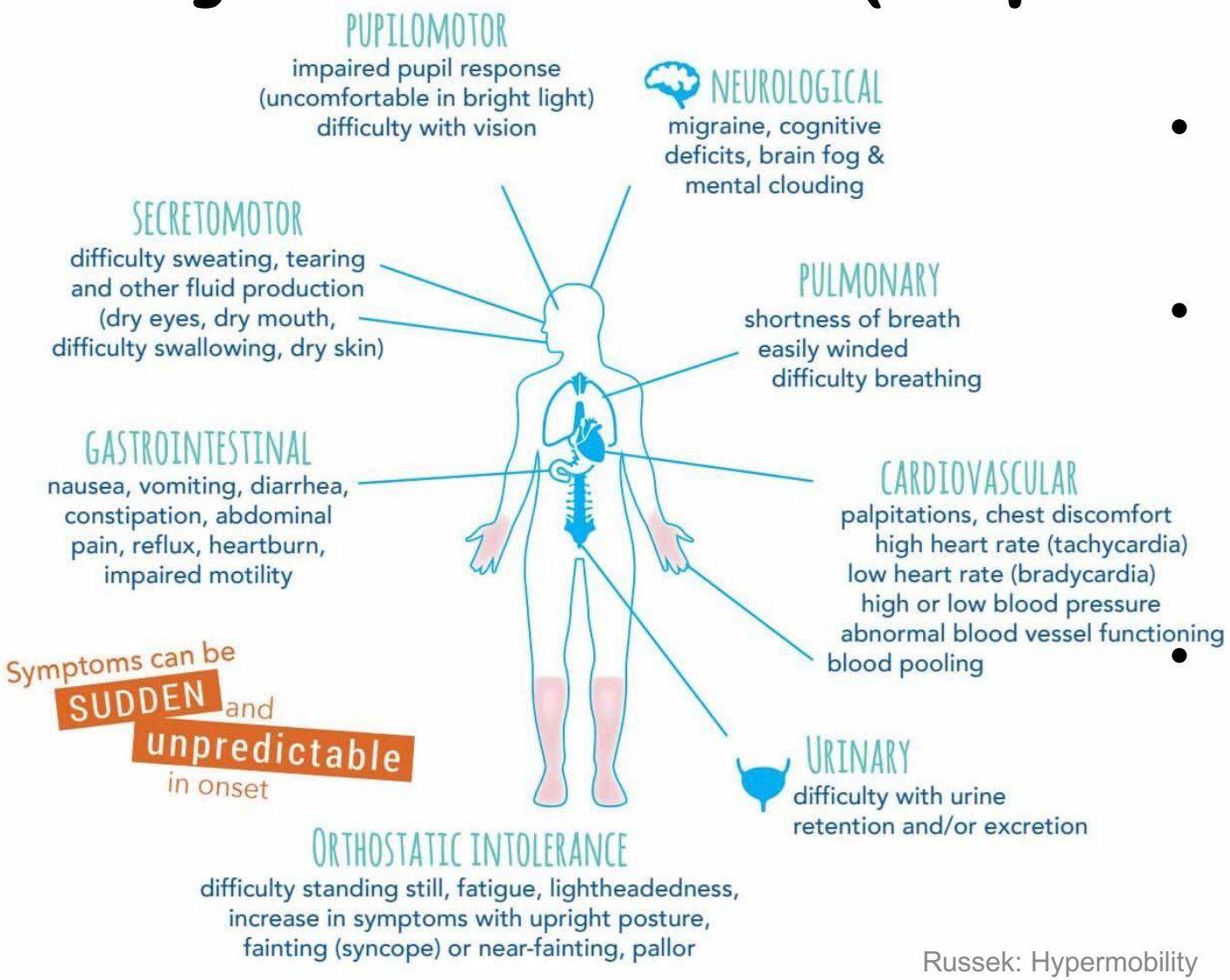
Mast Cell Activation Syndrome/Disorder

Postural Orthostatic Tachycardia Syndrome

Seneviratne, 2017; Hakim, 2017

Dysautonomia (especially POTS)

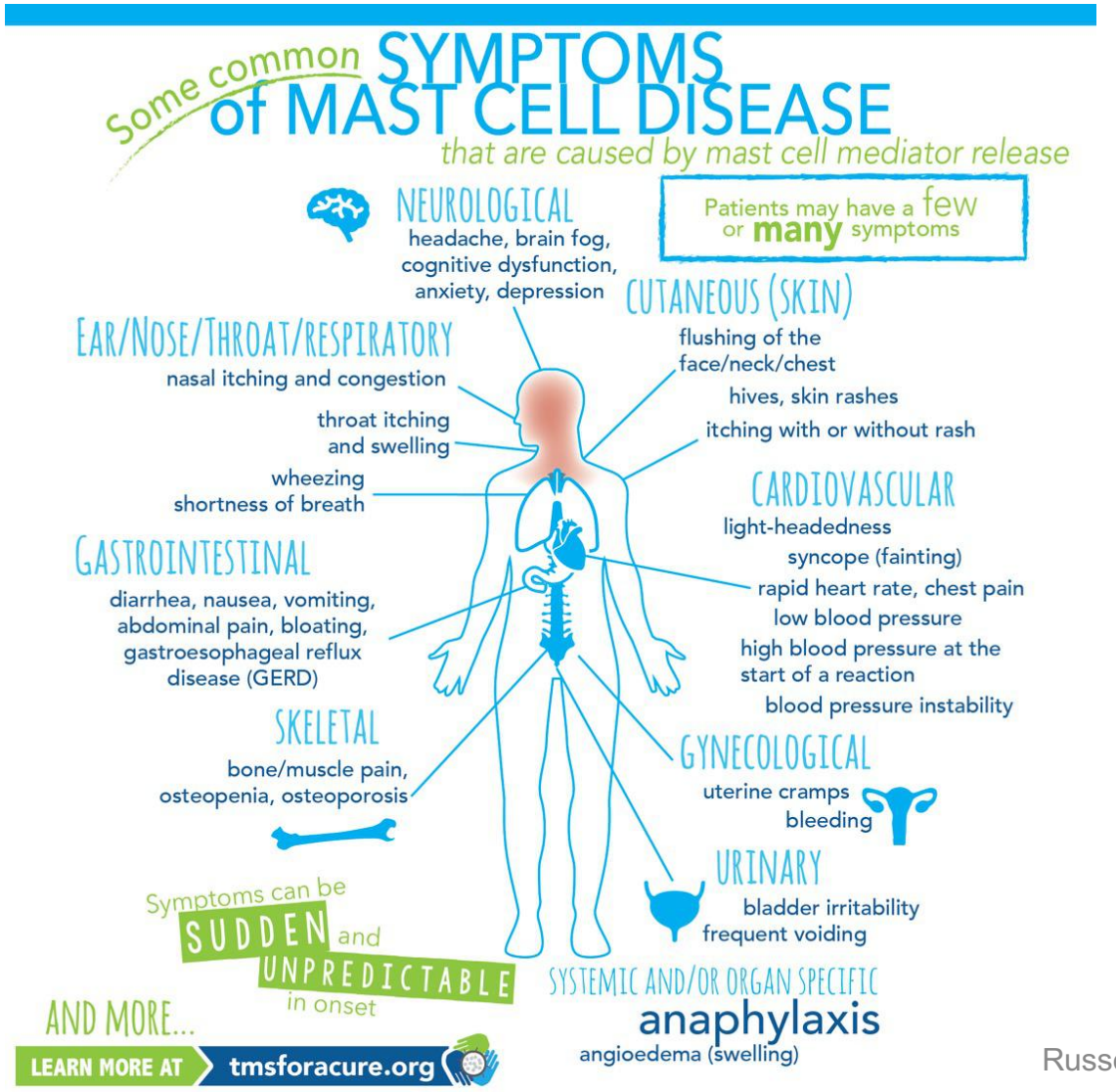
Overview of POTS



- HSD is a risk factor
  - Female:male ratio is 5:1
  - 62% of kids with POTS have HSD/hEDS
- Common triggers:
  - Puberty
  - Concussion
  - COVID
  - Deconditioning
  - Sleep disorders
- Different types of POTS: hypovolemic, neuropathic, MCAS, hyperadrenergic

Boris, 2021; Chen, 2020; Zhang, 2020; Bryarly, 2019

Mast Cell Activation Syndrome (MCAS)



Lab testing has very, very high false negative rates

- Possibly 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 parentera 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

- 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)
- Pseudo seizures/non-epileptic seizures, fainting and dystonia (muscle spasticity) may be due to cervical instability. (Russek, 2022)
  - MRI done supine with 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)
- Functional Neurological Disorders (FND) can occur in HSD, but look for other explanations first. (Fernandez, 2024)
- Patients may be anxious, but S&S are not necessarily caused by anxiety

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

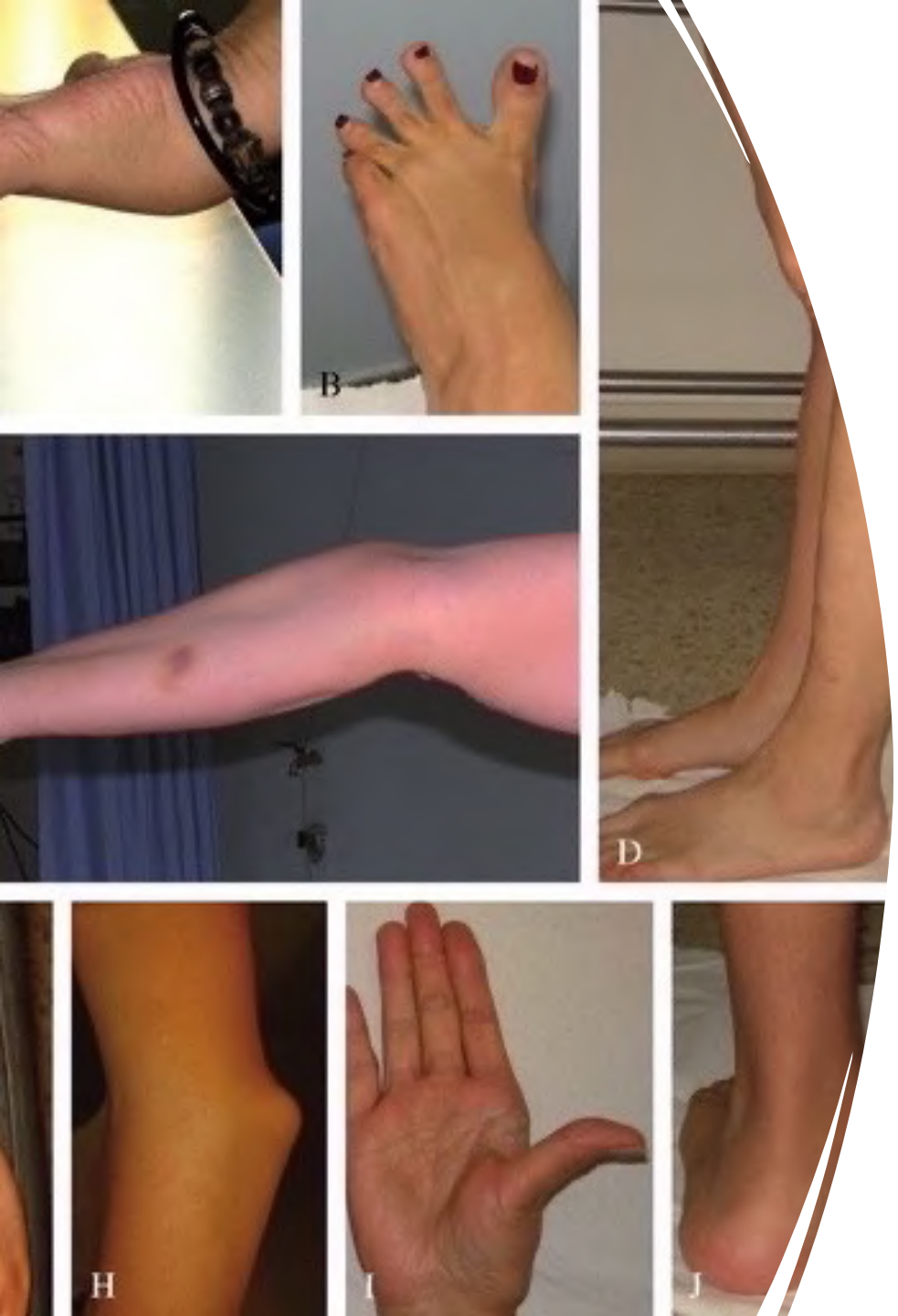
Gender Dysphoria

- 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

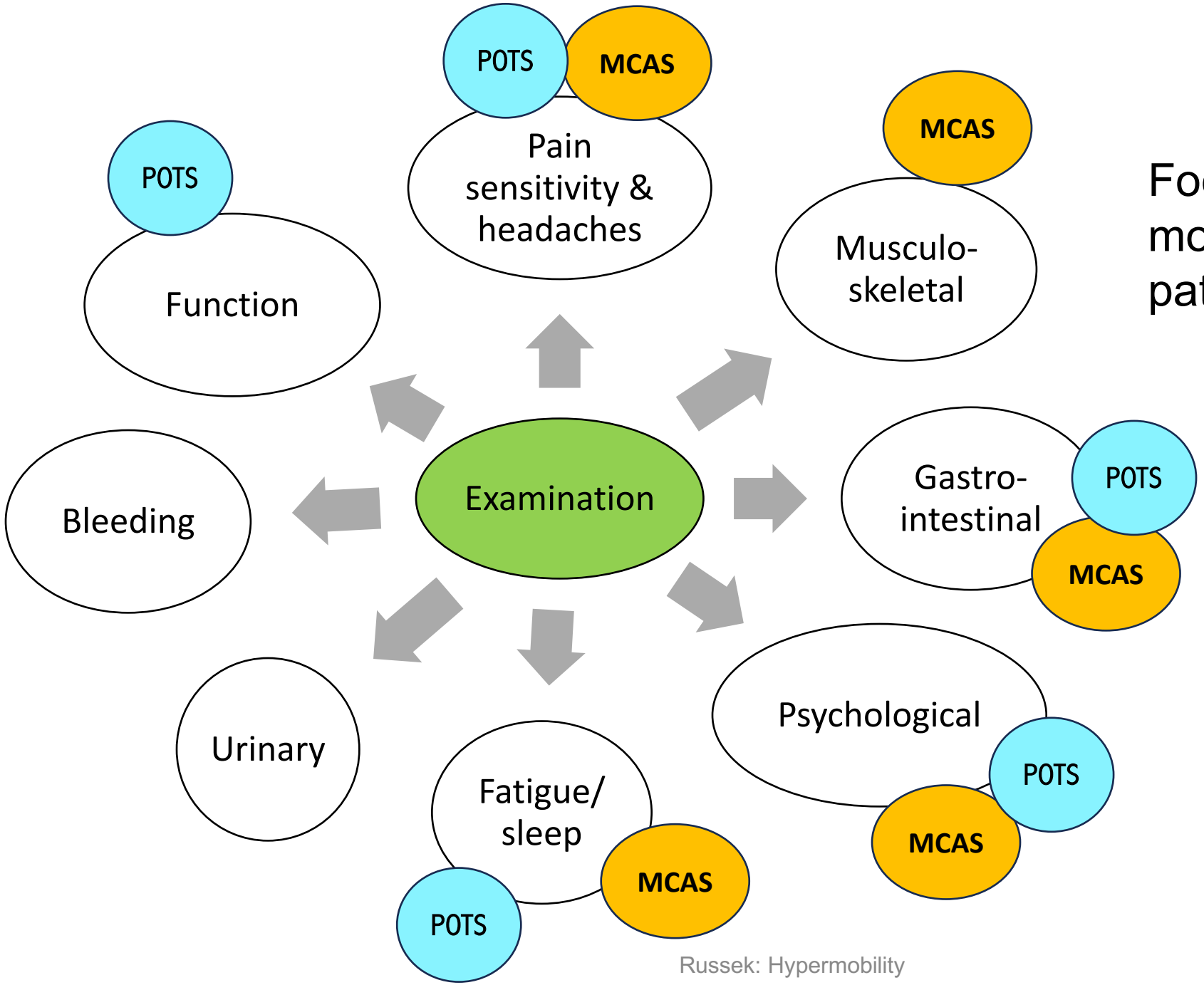
(Jones, 2022)

- A case series of patients transitioning from female to male
  - 3 patients had decreased POTS symptoms with testosterone therapy

(Boris, 2019)

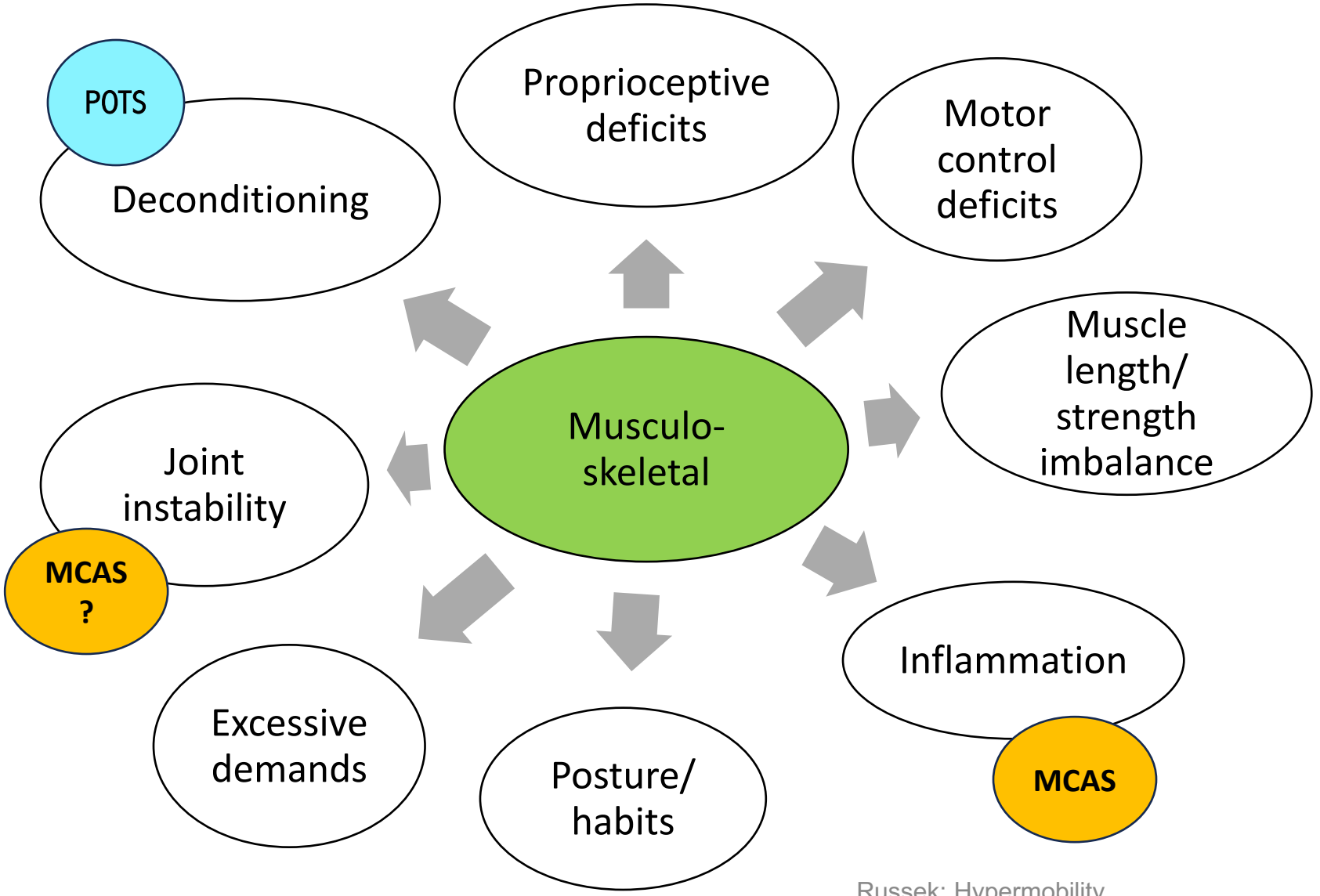


Examination of Patients with HSD



Focus on what is most important to the patient/family

Musculoskeletal & Function Problems



Look for 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…

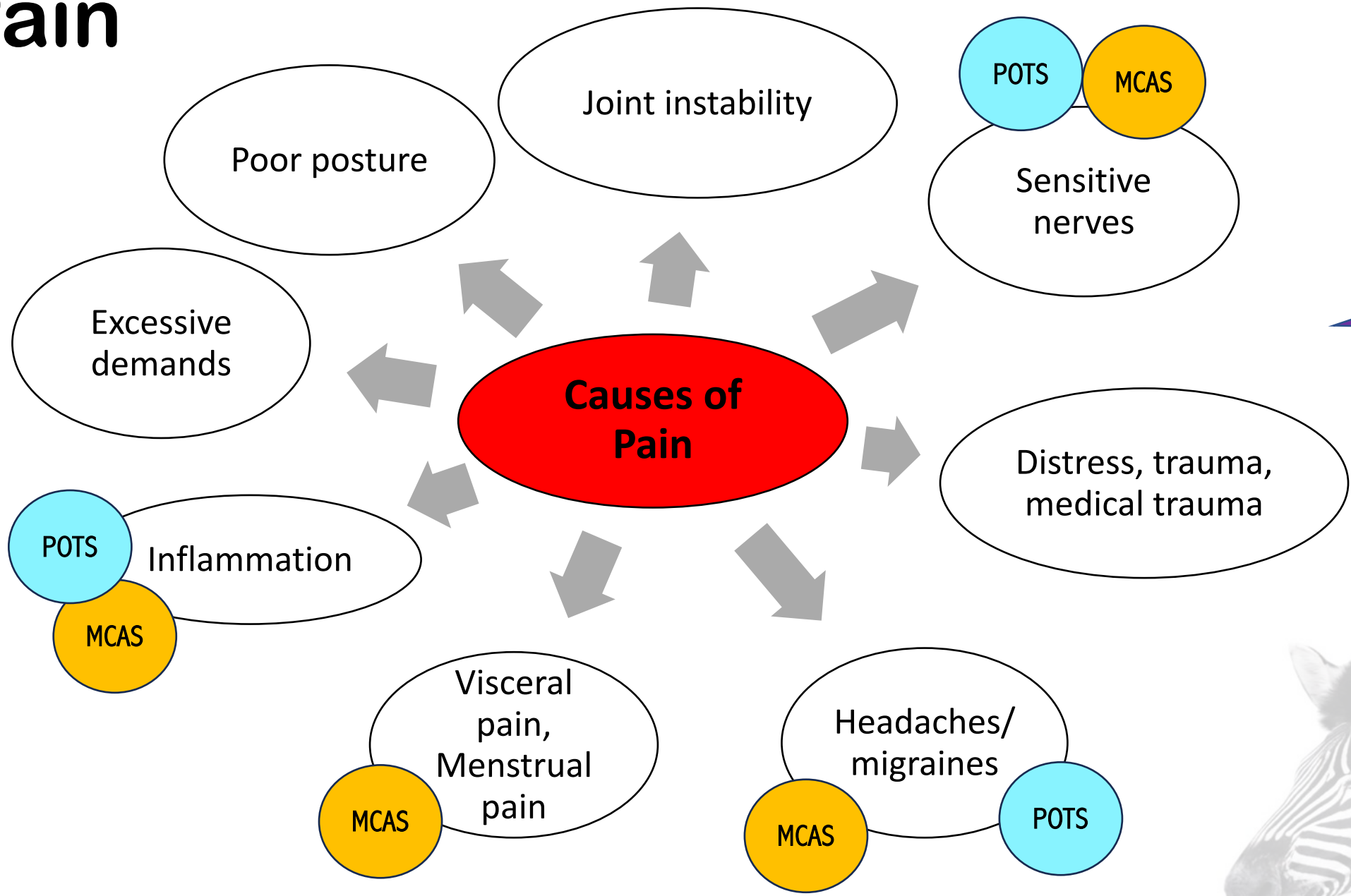
- The Beighton Score joints are only special for making an official diagnosis.
- Patients may be hypermobile in other joints, such as the shoulder, neck, lumbar spine, etc.
- Assess any joint that is problematic

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: alignment, proprioception, motor control, etc.
  - Factors causing local or systemic inflammation
  - Messed up volume control due to sensitization/nociplastic pain.

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

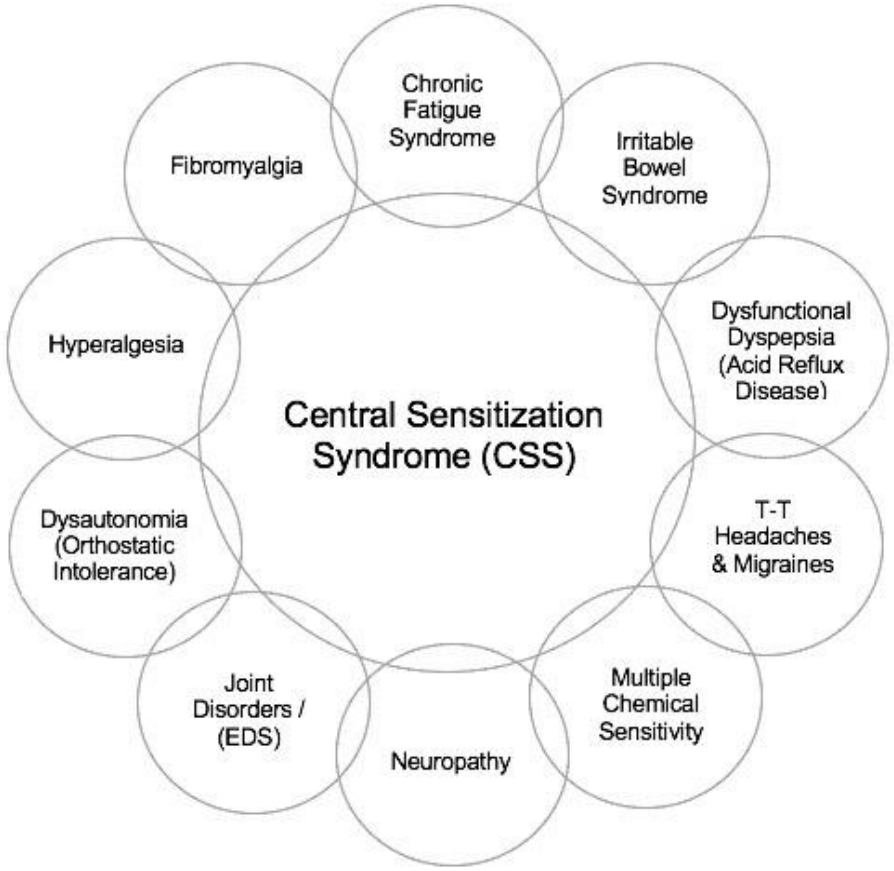
Pain



Several Pain Management Handouts

Daylor, 2023a; Junghans-Rutelonis , 2019; Revivo, 2019; Nicholson, 2022

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					

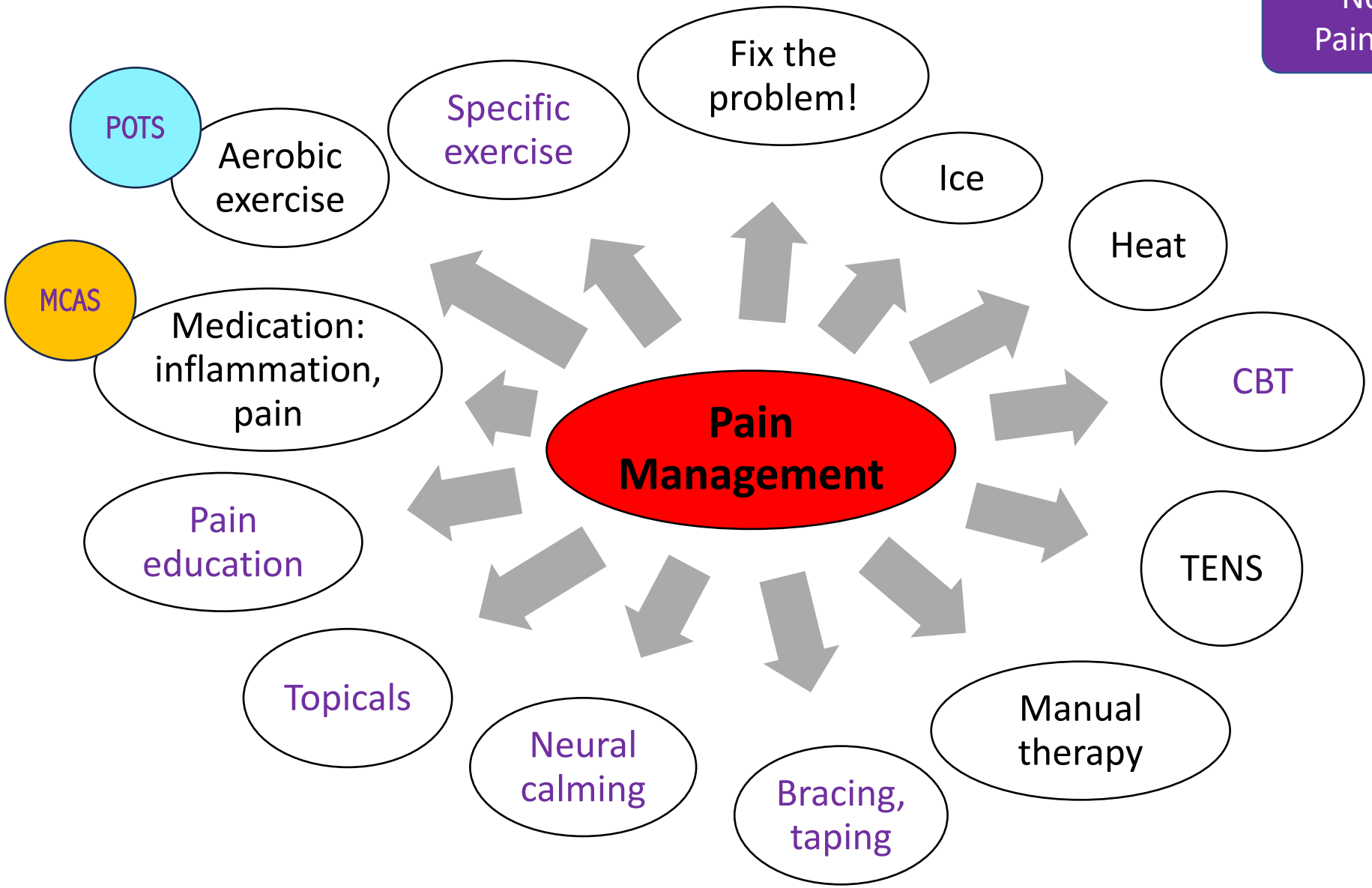
CSI-9 score

Subclinical	0-9
Mild	10-19
Mod/severe	20-36

(Nishigami, 2018)

Nociplastic Pain

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



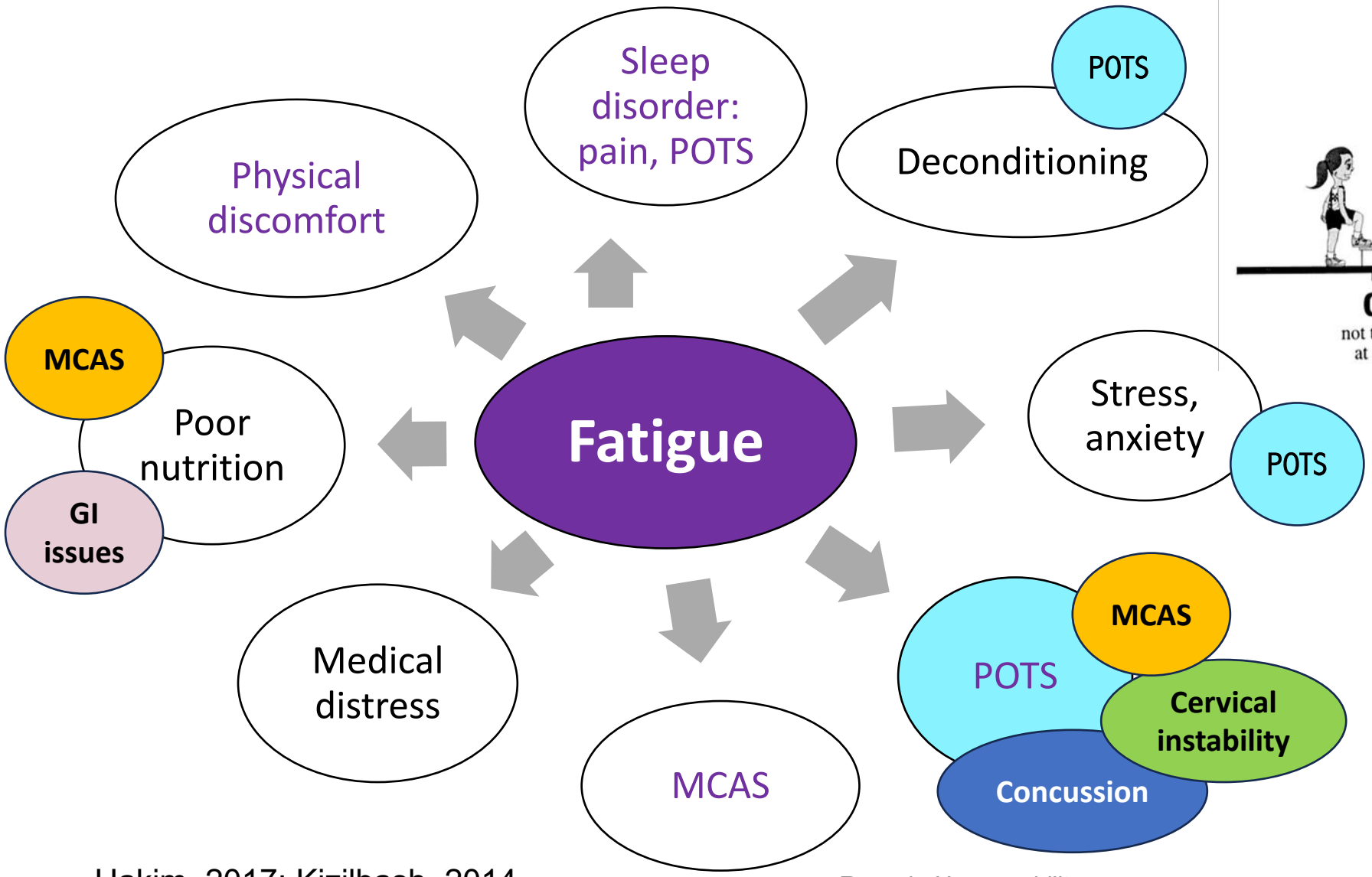
Nociplastic Pain
Pain Apps for Teens

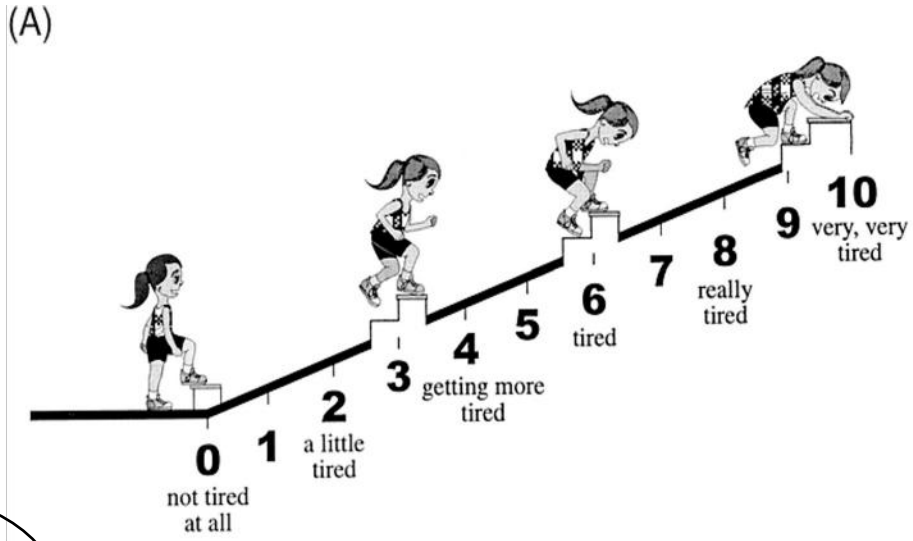
- Curable Pain CBT app (6 wks free)
- Free pain management apps for teens:
  - WebMAP
  - IBeatPain

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

Junghans-Rutelonis , 2019; Revivo, 2019; Nicholson, 2022; Daylor, 2023b

Fatigue/Sleep Problems





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

Hakim, 2017; Kizilbash, 2014

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://batemanhornecenter.org/wp-content/uploads/2016/09/NASA-LeanTest-Instructions-April-2018.pdf

(Physical Therapy) Management of HSD/hEDS

Russek: Hypermobility
https://www.physio.co.uk/what-we-treat/musculoskeletal/symptoms/hypermobility.php

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

Modified from model proposed by Jane Simmonds, DProf, MCSP, MACP, SFHEA, Univ. Coll. London

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

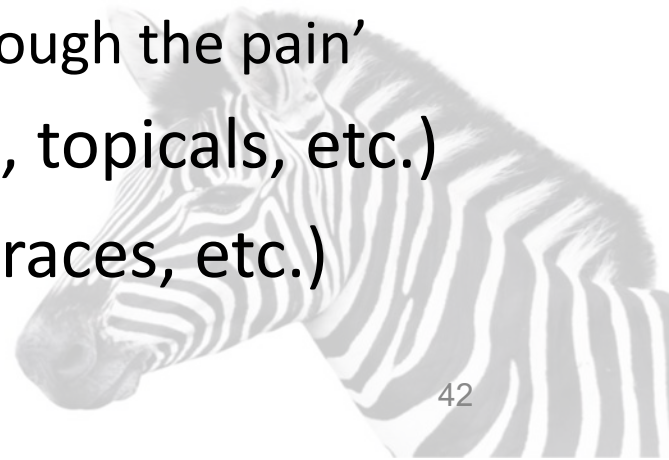
- Posture, joint protection, body mechanics, ergonomics
  - Orthotics, braces, & splints if/when needed
- Self-care, injury prevention, pain self-management
  - Problem-solving, braces, heat/ice, TENS, topicals, physiological quieting
- Appropriate exercise/activity
- Sleep hygiene & positioning; fatigue 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)

Pain Management Approach

HSD 103: Pain Management

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. Teach strategies to manage their pain (e.g., TENS, ice, topicals, etc.)
6. Optimize function (e.g., adapting the environment, braces, etc.)



Daylor, 2022a; Daylor, 2022b; Chopra, 2017

Joint Protection and Posture

HSD 105: Posture & Joint Protection

"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)

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

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)

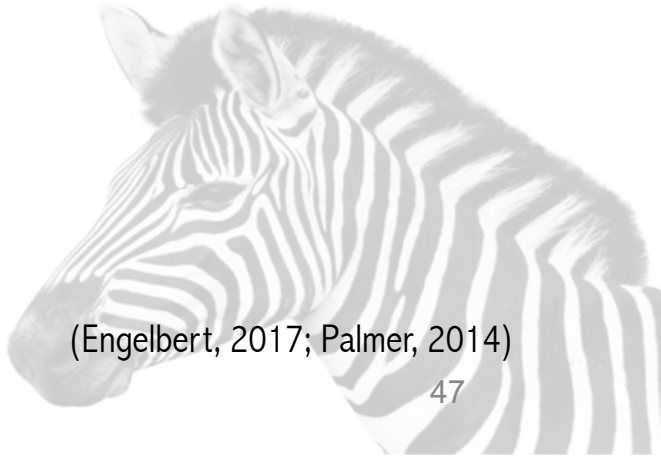
Thanks to Stephanie Carroll, RN, for suggesting these full body compression garments

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

Exercise Prescription

HSD 104: Exercise

- Proprioception, stabilization, motor control & coordination
  - Start movements from good alignment
  - Make sure every movement is being done correctly, 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)



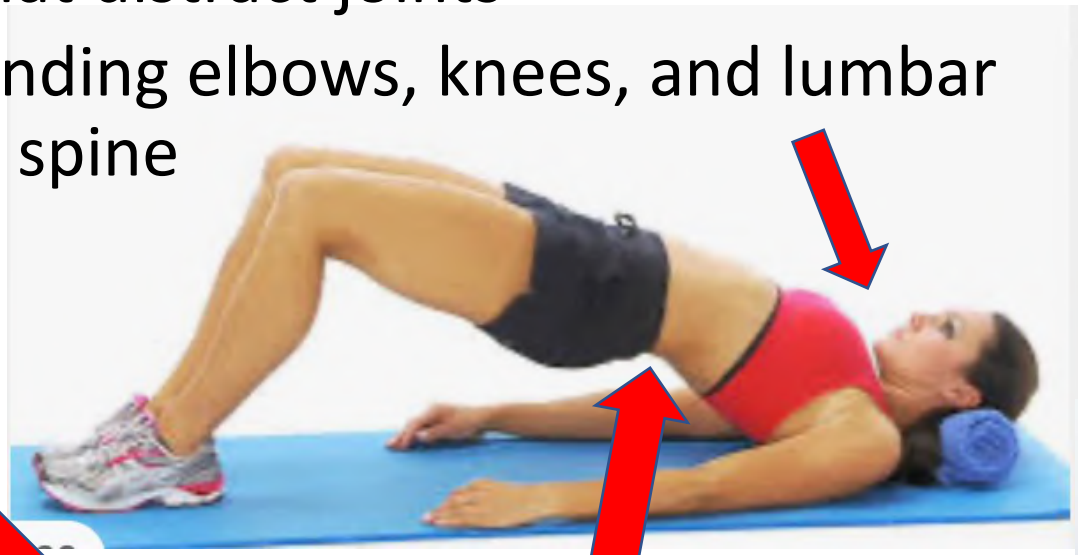
(Engelbert, 2017; Palmer, 2014)

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
- Lengthen tight muscles (while stabilizing joints) - controversial
- Both generalized fitness and patient-specific exercises help
- Start low, go slow!
- Exercises must be appropriate, not be too difficult, kids must be able to do them correctly, must have time & support

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

Evidence for Benefits of Exercise

- Research about exercise for kids with HSD is limited (Peterson, 2018)
- Exercise in kids and teens can decrease pain, improve function, decrease kinesiophobia and disability (Zibriskie, 2022; van Meulenbroek, 2020)
- Some studies of exercise in children & adolescents 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 kids, 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
- Using exercises that are boring or unpleasant
  - Standard adult exercises may be boring for kids

(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

Russek, 2019; Simmonds, 2022

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

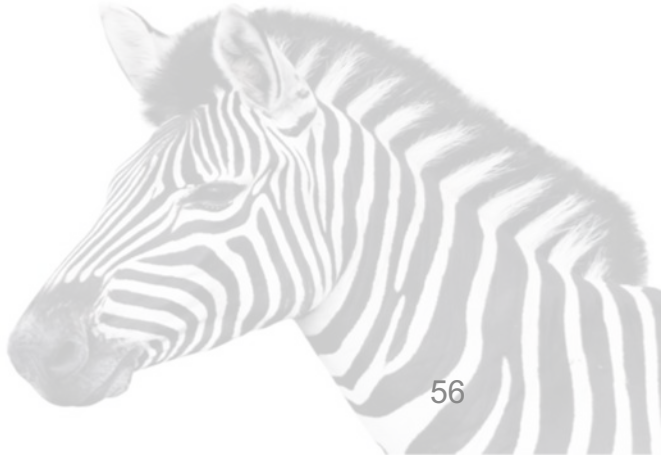
  (Revivo, 2019)
- Patient/family education benefits both children and parents

  (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

Chopra, 2017
Tinkle, 2017



Surgical/Hospital Precautions

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 Søborg, 2017; Burcharth, 2012)

Handout for patients to share with surgeons and anesthesiologists

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!	***In the unconscious HSD/hEDS patient, a little force may displace any joint.*** ***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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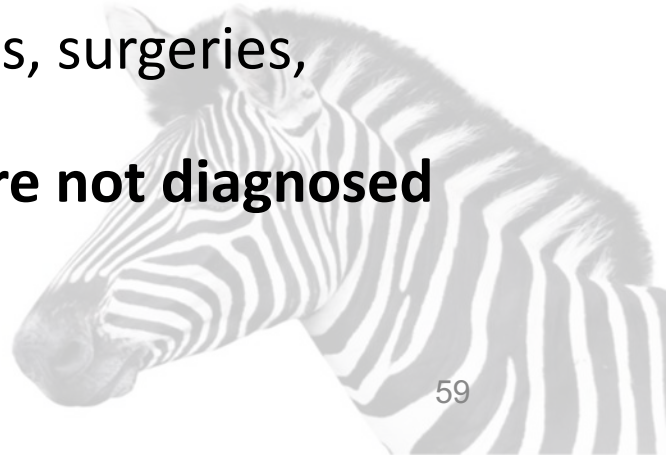
This document is online at *www.AlanSpanosMD.com*. It was updated March 2019.

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

- This handout should be at (but isn't at the moment):
- https://edswellness.org/wp-content/uploads/2019/07/7-Surgical-Anesthetic-Precautions.pdf
- Chronic Pain Partners has excellent patient handout at: https://www.chronicpainpartners.com/wp-content/uploads/2023/02/surgery-prep-meeting-your-eds-hospital-stay-needs.pdf
- I have a more technical handout for providers:
- https://webspace.clarkson.edu/~lrussek/docs/hypermobility/SurgeryHSD.pdf

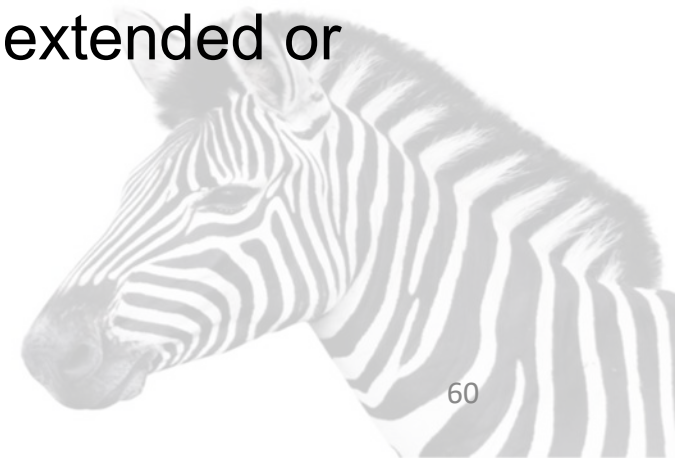
What Can YOU do for These Patients?

- 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, physical medicine, rheumatologists, neurologists, allergists/immunologists, GI, hematologists, psychologists, etc…
- Provide safe treatment
- 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**



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
  - Patients 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

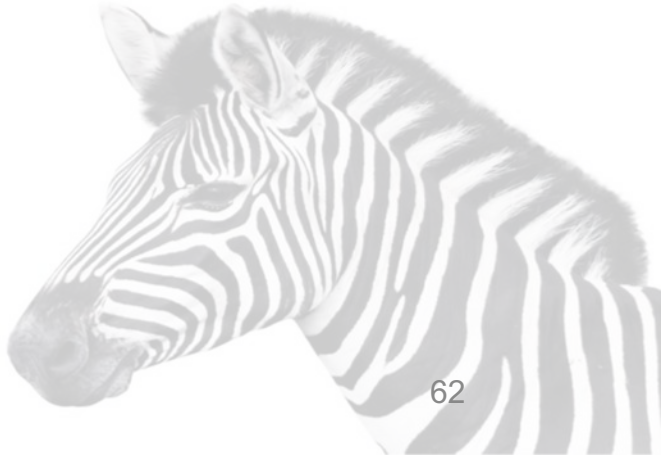
- https://webspace.clarkson.edu/~lrussek/research.html

Available on my website

- 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

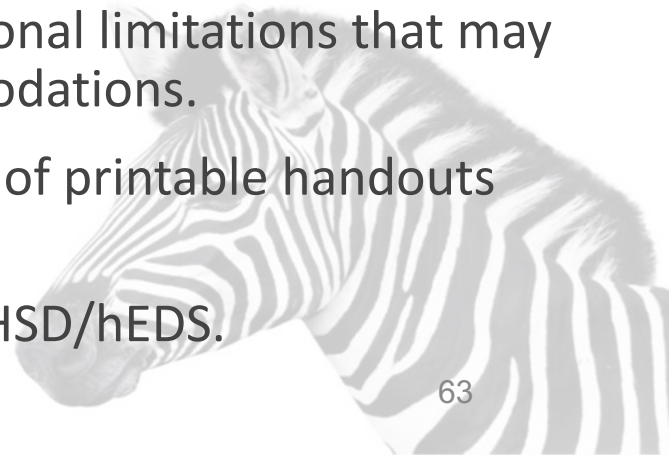
Hypermobility Lecture Series Schedule

- 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 with HSD, POTS, MCAD



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.

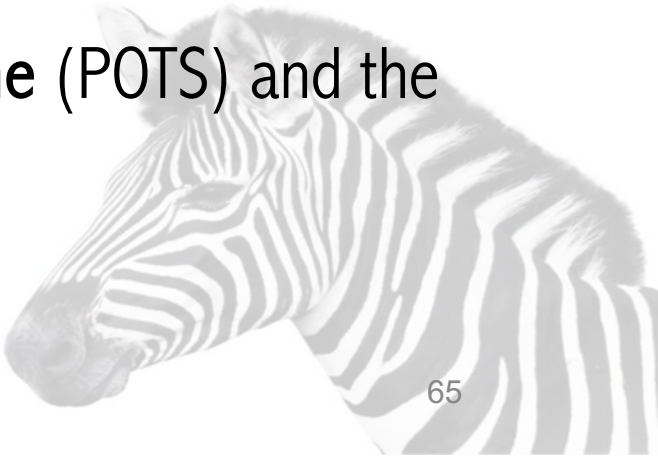


Resources for POTS

- **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

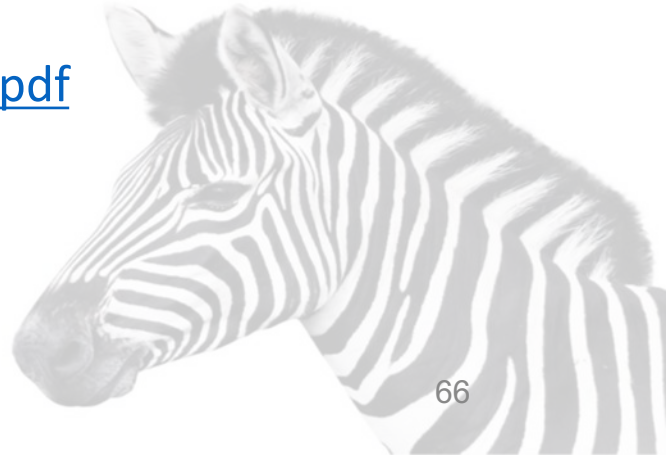
Resources for GI Problems

- 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/



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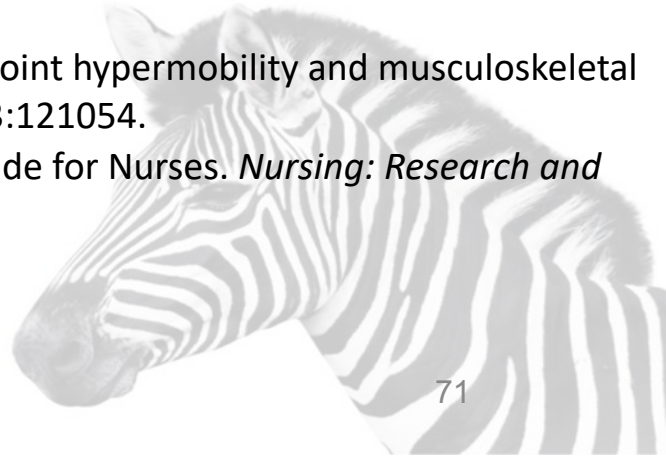

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Thank You!

Questions?