Hypermobile Ehlers-Danlos Syndrome (hEDS)

A Patient Guide for Cardiologists

WHAT IS hEDS? hEDS is a heritable disorder of connective tissue, the structural 'glue' of the body, causing joint instability, skin fragility, and systemic effects. Severity varies widely, from mild laxity and intermittent bracing to wheelchair use and complex multisystem involvement.

~1 in 500 people affected	Avg. 10+ years to diagnosis	3:1 to 4:1 diagnosed are female	No cure: management-focused

HOW HEDS AFFECTS THE BODY — SYSTEMIC INVOLVEMENT:

Patient has checked applicable symptoms

Neurological

- ☐ Migraines & headaches
- ☐ Brain fog/cognitive fatigue
- ☐ Small fiber neuropathy
- ☐ Proprioception deficits
- ☐ Anxiety/depression (often neurological in origin)

Gastrointestinal

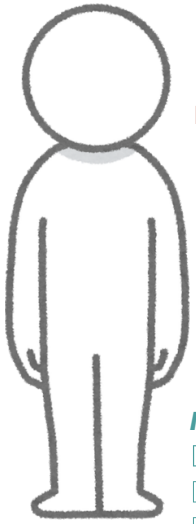
- ☐ IBS
- ☐ Gastroparesis/ delayed emptying
- ☐ GERD & acid reflux
- ☐ Food intolerances

Immune / MCAS

- ☐ MCAS — mast cell overactivation
- ☐ Flushing, hives, itching
- ☐ GI distress & food reactions
- ☐ Chemical/environmental sensitivity

Genitourinary

- ☐ Pelvic floor dysfunction
- ☐ Bladder urgency/frequency
- ☐ Chronic pelvic pain
- ☐ Menstrual irregularities



Cardiovascular

- ☐ POTS — heart rate spikes on standing
- ☐ Blood pooling & dizziness
- ☐ Palpitations

Dermatological

- ☐ Soft, velvety, hyperextensible skin
- ☐ Stretch marks without weight change
- ☐ Easy bruising
- ☐ Poor wound healing

Fatigue & Sleep

- ☐ Profound fatigue
- ☐ Non-restorative sleep
- ☐ Post-exertional malaise
- ☐ Chronic widespread pain at rest

Musculoskeletal

- ☐ Joint hypermobility & instability
- ☐ Subluxations & dislocations
- ☐ Chronic widespread pain
- ☐ Muscle fatigue & weakness
- ☐ Cervical instability (can cause neurological issues)

DO

- Assess orthostatic vitals. Supine measurements alone will miss significant dysautonomia
- Treat POTS as an autonomic condition, not a psychological one
- Consider full POTS medication toolkit: beta blockers, ivabradine, fludrocortisone, and midodrine depending on presentation
- Increase sodium and fluid intake as a first-line intervention
- Coordinate with neurology, rheumatology, and pain management
- Screen for MCAS as a cardiovascular symptom amplifier: Flushing, palpitations, and blood pressure instability can have mast cell origins

DON'T

- Advise standard aerobic exercise protocols without dysautonomia-specific modification
- Rely solely on supine heart rate and blood pressure measurements
- Assume POTS is a standalone diagnosis without investigating for underlying hEDS
- Discharge with "nothing cardiac found" without evaluating for dysautonomia
- Attribute palpitations and chest symptoms to panic disorder without orthostatic assessment
- Tell a patient to exercise more without a structured, autonomic-aware protocol

CONSIDER / REFER

- Tilt table test for formal POTS diagnosis
- Ivabradine for inappropriate sinus tachycardia and POTS: well-tolerated in hEDS
- Beta blockers (low-dose propranolol or metoprolol) for heart rate management
- Fludrocortisone for volume expansion in low-flow POTS
- Midodrine for blood pooling and orthostatic hypotension
- Recumbent or semi-recumbent exercise protocol (rowing, swimming, cycling) before upright exercise
- Neurology for dysautonomia evaluation if autonomic neuropathy is suspected
- Allergy/Immunology if MCAS is contributing to cardiovascular symptoms
- Compression garments for blood pooling; waist-high, 30-40mmHg
- While aortic involvement is more characteristic of vascular EDS (vEDS), a subset of hEDS patients demonstrate aortic root dilation. Obtain baseline echocardiogram if not previously done. Repeat imaging is warranted if the patient reports chest pain, new palpitations, or family history of aortic dissection.

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POTS, hEDS, and the Anxiety Misdiagnosis: POTS (Postural Orthostatic Tachycardia Syndrome) is diagnosed when heart rate increases 30 or more beats per minute upon standing, or exceeds 120 BPM, within ten minutes of orthostatic challenge. It is a measurable, physiological autonomic dysfunction. It is not anxiety. It disproportionately affects young women, which has historically contributed to its dismissal. In hEDS, lax connective tissue allows blood to pool in the lower extremities on standing, reducing venous return and triggering compensatory tachycardia. A patient who reports dizziness, palpitations, brain fog, and exercise intolerance that worsens on standing deserves orthostatic assessment before psychological explanation is considered.

Why "Exercise More" Can Harm POTS Patients with hEDS: Exercise intolerance in hEDS-associated POTS is physiological, not motivational. Upright exercise in an unmanaged POTS patient can trigger significant symptom flares, cardiac stress responses, and post-exertional malaise that sets the patient back for days. The standard cardiac advice to increase aerobic activity is contraindicated until dysautonomia is adequately managed. When exercise is introduced, it must begin in a recumbent or semi-recumbent position: rowing, swimming, and recumbent cycling are the established starting points. Upright exercise is reintroduced gradually as orthostatic tolerance improves. Compression garments and sodium loading before exercise sessions improve tolerance **significantly**.

Hyperadrenergic POTS: A subset of POTS patients present with elevated norepinephrine on standing (>600 pg/mL), paradoxical hypertension, and worsening symptoms with beta blockers. If standard POTS treatment is ineffective or symptoms worsen with propranolol/metoprolol, consider hyperadrenergic subtype. Clonidine may be more appropriate than standard beta blockade. Refer to autonomic neurology if hyperadrenergic POTS is suspected.

MAST CELL ACTIVATION SYNDROME (MCAS) — CARDIOVASCULAR RELEVANCE

MCAS is estimated in a significant subset of hEDS patients and directly compounds cardiovascular instability

Cardiovascular Symptoms of MCAS

- Flushing episodes, often without obvious trigger
- Tachycardia and palpitations after exposure to triggers
- Sudden hypotension/near syncope
- Chest tightness/pressure (nonstructural)
- Anaphylactoid reactions with hemodynamic instability
- Worsening of POTS symptoms after food, scent, or temp triggers
- Highly variable day-to-day cardiovascular stability

MCAS Triggers Relevant to Cardiology

Triggers that provoke MCAS-driven cardiovascular instability:

- Heat, exertion, or rapid temp change
- Contrast dyes: risk of severe reaction; pre-medicate
- NSAIDs and certain medications
- Stress (physical or emotional)
- Certain foods
- Fragrances + chemical exposures
- Pre-menstrual hormonal shifts

Clinical Note

When POTS symptoms are highly variable, episodic, or treatment-resistant, consider MCAS as a co-driver. H1+H2 antihistamines may reduce cardiovascular instability independently of standard POTS management. Refer to Allergy/Immunology familiar with MCAS.

Contrast Dye Caution

hEDS patients with MCAS are at elevated risk of contrast reactions. Consider pre-medication protocol (corticosteroid + antihistamine) before contrast procedure.

POTS and MCAS: A Bidirectional Relationship: These conditions do not simply co-occur. They amplify each other. Autonomic dysfunction activates mast cells through sympathetic signaling, increasing mediator release. Mast cell mediators in turn cause vasodilation and histamine-driven tachycardia that destabilizes autonomic function. This feedback loop explains why symptoms are often disproportionate, highly variable, and resistant to single-condition treatment. Providers should consider parallel management of both conditions rather than sequential treatment.

POTS & DYSAUTONOMIA IN hEDS — WHY THEY OCCUR

Structural Mechanisms

- **Vascular laxity:** Defective collagen in vessel walls impairs venous tone, causing excessive blood pooling in the lower extremities on standing
- **Reduced venous return:** Pooling triggers compensatory tachycardia; the heart rate spike is a consequence, not the primary problem
- **Small fiber neuropathy:** Autonomic nerve fiber damage impairs vasoconstriction and baroreceptor signaling
- **Hypovolemia:** Chronic low blood volume is frequent in hEDS/POTS; vascular laxity reduces effective circulating volume
- **Mast cell co-activation:** MCAS-related mediator release causes additional vasodilation and hemodynamic instability

Common Presentations

- Heart rate increase of 30+ bpm on standing (40+ bpm in those under 19)
- Orthostatic tachycardia without orthostatic hypotension
- Presyncope/syncope on standing/prolonged upright posture
- Palpitations: often positional or exertion-related
- Exercise intolerance disproportionate to deconditioning
- Brain fog, cognitive slowing, visual disturbance on standing
- Blood pooling: visible livedo reticularis, dependent edema
- Chest pain/pressure (not structural; autonomic origin)
- Nausea and GI symptoms worsened by upright posture
- Temperature dysregulation and sweating abnormalities

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COMMON MISDIAGNOSES IN hEDS PATIENTS PRESENTING TO CARDIOLOGY		
Often Diagnosed As	**Consider Instead/Also**	**Key Differentiator**
Deconditioning	POTS from vascular/autonomic dysfunction	HR increase on standing 30+ bpm; symptoms predate inactivity
Anxiety/panic disorder	POTS or MCAS-driven cardiovascular instability	Positional HR changes; symptom pattern linked to posture or triggers
Inappropriate sinus tachycardia	POTS	Orthostatic component; full 10-min standing HR assessment
Vasovagal syncope (isolated)	hEDS dysautonomia + POTS	Episode pattern; connective tissue features
Cardiac arrhythmia	Autonomic-driven tachycardia/ MCAS flushing + palpitations	Holter often unremarkable; tilt table test; MCAS workup
Functional/medically unexplained	hEDS with POTS and/or MCAS	Full connective tissue history; validated POTS diagnostic criteria

MY CURRENT MEDICATIONS & SUPPLEMENTS	WHAT HELPS:
	WHAT MAKES IT WORSE:

WHAT I NEED FROM TODAY'S APPOINTMENT
My primary concern today:
Questions I have:
Medication changes:
Referrals needed:
Other:

CURRENT SYMPTOM SEVERITY: Complete this section using the Mankoski Pain Scale (pg. 4)
Heart rate/palpitation frequency and severity:
MCAS/flushing/reaction frequency and severity:
Presyncope/syncope frequency and severity:
Exercise intolerance frequency/severity:
Additional Symptoms:

Sources: Malfait et al. 2017 (AJMG) | Tinkle et al. 2017 (AJMG) | Sheldon et al. 2015 POTS consensus | Raj 2013 (Circulation) | Afrin et al. 2017 (Immunol Allergy Clin) | Benarroch 2012 (Neurology) | ehlers-danlos.com | [illegible] | [illegible]

This document was created to provide a focused cardiovascular reference for providers less familiar with hEDS and its autonomic manifestations. It is evidence-based and designed to support efficient, informed care.

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MANKOSKI PAIN SCALE

Use this scale when rating your pain severity in CURRENT SYMPTOM SEVERITY

#	What the pain is like	Typical treatment	In my own words
0	No pain.	*No medication needed.*	*"I feel completely normal."*
1	Very minor annoyance -- occasional minor twinges.	*No medication needed.*	*"Hardly notice it."*
2	Minor annoyance -- occasional strong twinges.	*No medication needed.*	*"Annoying but manageable."*
3	Annoying enough to be distracting.	*Mild OTC painkillers may help.*	*"Hard to ignore; affects my focus."*
4	Can be ignored if very focused, but still distracting.	*Mild OTC painkillers relieve pain for 3-4 hours.*	*"Getting in the way of tasks."*
5	Can't be ignored for more than 30 minutes.	*Mild OTC painkillers reduce pain for 3-4 hours.*	*"Stops me mid-task."*
6	Can't be ignored. Can still go to work and participate in social activities.	*Stronger prescription pain relief needed; works 3-4 hours.*	*"Present all the time. I push through."*
7	Difficult to concentrate; interferes with sleep. Can still function with effort.	*Stronger painkillers only partially effective.*	*"Hard to function. Sleep is disrupted."*
8	Physical activity severely limited. Can read/converse with effort. Nausea possible.	*Strongest painkillers minimally effective.*	*"Mostly bed-bound. May feel nauseated."*
9	Unable to speak. Crying out or moaning uncontrollably. Near delirium.	*Strongest painkillers only partially effective.*	*"Cannot communicate. Losing control."*
10	Unconscious. Pain causes passing out.	*Strongest painkillers only partially effective.*	*"Passed out or on the verge of it."*

Mankoski Pain Scale developed by Andrea Mankoski, 1995. Adapted for patient communication. Not a clinical diagnostic tool.

IMPORTANT NOTE FOR HEDS PATIENTS & PROVIDERS:

People with hEDS often have an altered pain baseline due to central sensitization -- a process in which the nervous system becomes increasingly sensitized to pain signals over time.

A "5" for this patient may be what others feel as a "8."
Please do not compare severity numbers to those of patients without chronic illness.

This scale helps us communicate:
it is not a measure of tolerance, willpower, or how "bad" things really are.