Hypermobile Ehlers-Danlos Syndrome (hEDS)

A Patient Guide for Pain Management Specialists

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

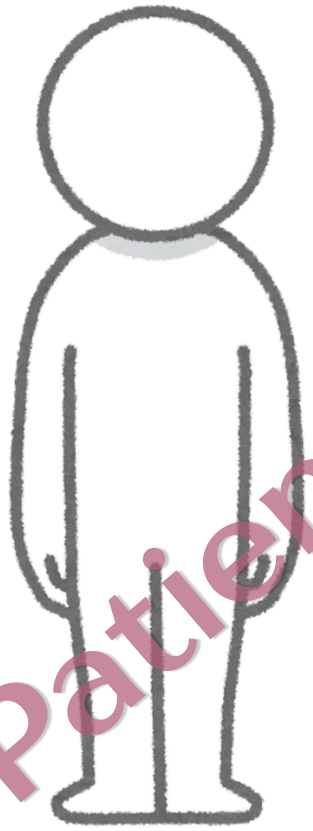
- ☐ IBS
- ☐ Gastroparesis/ delayed emptying
- ☐ GERD & acid reflux
- ☐ Food intolerances

Immune / MCAS

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

Fatigue & Sleep

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



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

Genitourinary

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

Musculoskeletal

- ☐ Chronic widespread pain
- ☐ Subluxations & dislocations
- ☐ Muscle fatigue & weakness
- ☐ Joint hypermobility & instability
- ☐ Cervical instability (may contribute to headache, cranial nerve symptoms, or myelopathy)

The hEDS Trifecta: Frequently Co-Occurring Conditions

hEDS	+	POTS	+	MCAS
Joint instability Structurally abnormal connective tissue Systemic symptoms		Heart rate spikes on standing Dizziness & fatigue Brain fog & cognitive dysfunction Exercise intolerance		Mast cell overactivation Flushing, hives, itching GI distress & food reactions Chemical/environmental sensitivity

Central Sensitization, Opioids, and hEDS: Pain in hEDS is not purely mechanical. Central sensitization, in which the nervous system becomes progressively more reactive to pain signals, is common and changes the treatment calculus significantly. Long-term opioid use can worsen central sensitization through opioid-induced hyperalgesia, making pain harder to manage over time. Low-dose naltrexone works through a different mechanism, modulating glial cell activity and neuroinflammation, and is increasingly used in hEDS and fibromyalgia with a favorable side effect profile. hEDS patients are frequently undertreated after years of being dismissed; the goal is effective, evidence-informed multimodal pain management, not gatekeeping. Wind-up phenomenon and allodynia, pain triggered by normally non-painful stimuli such as light touch or clothing contact, are clinical markers of central sensitization and common in hEDS.

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: Rate 0-10 using the Wanbook Pain Scale (pg. 4)

Current pain severity:

Joint pain and instability location and pain severity:

Fatigue severity:

GI symptoms type and frequency:

Heart rate and dizziness triggers and frequency:

Additional symptoms or concerns:

DO

- Recognize central sensitization as a primary pain driver in hEDS
- Treat pain as multimechanistic. Nociceptive, neuropathic, + central components often coexist
- Assess for allodynia and wind-up phenomenon. Both indicate central sensitization and should inform treatment selection
- Address sleep dysfunction. Non-restorative sleep amplifies central sensitization significantly
- Coordinate with rheumatology, neurology, PT, + psychology
- Consider LDN as an adjunct. Emerging evidence supports its use in central sensitization + chronic pain
- Validate pain severity even when the patient appears functional
- Assess POTS + MCAS as pain amplifiers. Autonomic dysfunction + mast cell activation worsen pain perception
- Be aware that MCAS flares can trigger acute pain episodes that may mimic other conditions. Mast cell activation lowers pain thresholds systemically.

DON'T

- Default to opioids as first-line treatment. They can worsen central sensitization over time
- Dismiss pain severity because labs and imaging are normal
- Treat pain in isolation w/o addressing autonomic + immune comorbidities
- Assume the patient is drug-seeking because they have tried many medications
- Interpret a patient's ability to function as evidence their pain is manageable
- Use pain contracts or surveillance frameworks disproportionately. hEDS patients are undertreated, not overtreated
- Recommend high-impact exercise or standard physical conditioning protocols
- Proceed with local anesthetic procedures without awareness of possible local anesthetic resistance. Some hEDS patients require higher doses or alternative agents for adequate effect.

CONSIDER / REFER

- Low dose naltrexone (LDN). Emerging evidence for central sensitization and neuroinflammation
- Ketamine infusion therapy for refractory central sensitization
- Tricyclic antidepressants or SNRIs for neuropathic + central pain components
- Psychology/pain psychologist for cognitive behavioral approaches to chronic pain
- PT specializing in hypermobility and the Muldowney Protocol
- Sleep specialist if non-restorative sleep isn't responding to standard interventions
- Neurology if small fiber neuropathy has not been evaluated
- Interventional and topical options: nerve blocks for localized pain; compounded analgesics (lidocaine, ketamine, or gabapentin cream) to reduce systemic medication burden
- Anesthesia consultation prior to surgical procedures. hEDS patients may exhibit local anesthetic resistance and atypical responses to sedation.

Local Anesthetic Resistance in hEDS: Some hEDS patients exhibit reduced or absent response to standard local anesthetics, including lidocaine. The mechanism is not fully understood but may relate to connective tissue structure and mast cell involvement. If a procedure is not achieving expected analgesia, consider higher concentrations, alternative agents, or anesthesia consultation before concluding the patient is not responding appropriately.

Sources: Malfait et al. 2017 (AJMG) | Tinkle et al. 2017 (AJMG) | Genetics in Medicine Open 2025 | ehlers-danlos.com | [illegible] | [illegible]

This document was created to provide a pain-focused clinical reference for providers less familiar with hEDS.
Pain in this condition is multimechanistic and frequently undertreated — this reference is intended to support evidence-informed management.

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 Andrew 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 "9."
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.