Title: Recognizing and Effectively Managing Hypermobility-Related Conditions

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Abstract

Hypermobility Spectrum Disorder (HSD) and hypermobile Ehlers-Danlos Syndrome (hEDS) can cause widespread or chronic pain, fatigue, proprioceptive and coordination deficits resulting in functional restrictions. These conditions are common and often unrecognized, and patients are likely to present in physical therapy for musculoskeletal injuries, pain, or coordination deficits. Although physical therapy is considered central to managing these conditions, many patients report pain and iatrogenic injuries due to inappropriate interventions. The diagnostic classification for these conditions was revised in 2017 to supersede previous diagnostic categories of Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome – hypermobility type/type III. It is now known that these conditions affect multiple body systems and not just joints, and that patients require a holistic approach. This perspective article will describe the 2017 diagnostic classification system, clinical presentation, examination, evaluation, and management of patients with HSD/hEDS. Both adult and pediatric cases are presented to illustrate the patient management concepts discussed. This knowledge may lead to more effective management of this patient population.

Joint hypermobility-related disorders exist on a spectrum, ranging from asymptomatic generalized laxity (aka Generalized Joint Laxity) to symptomatic hypermobility that previously went by names such as Joint Hypermobility Syndrome (JHS or HMS) or Ehlers Danlos Syndrome hypermobility type or type III (EDS-HT or EDS-III).[1] In the past decade, researchers and clinicians have determined that we cannot distinguish between what used to be called JHS and EDS-HT and have defined a more restrictive diagnosis of hypermobile Ehlers Danlos Syndrome (hEDS) and less restrictive diagnosis of Hypermobility Spectrum Disorder (HSD). Formal diagnostic criteria for HSD have not yet been defined, but experts propose that HSDs are present in patients who are hypermobile, have musculoskeletal manifestations (either of hEDS[1] or more broadly[2]), and those manifestations cannot be explained by another diagnosis.[1,2] The current discussion refers to both HSD and hEDS (HSD/hEDS) unless noted otherwise; note that most research cited used prior diagnostic criteria for JHS or EDS-HT.

Joint hypermobility related conditions are likely to be the most common inherited connective tissue disorder, perhaps 100 times more common than rheumatoid arthritis[1] and almost as common as fibromyalgia.[3] Prevalence using the new diagnostic criteria is not yet known, but hypermobility is believed to affect as many as 10 million individuals in the U.S.[4] In Britain, which has prevalence data, JHS was found in 30% of adult patients presenting to a primary care clinic,[5] and 39% and 37% of adults seen in pain management and rheumatology clinics, respectively.[6] Even though joint hypermobility may be asymptomatic, it is often associated with symptoms that lead individuals to seek out health care. In spite of its prevalence, experts assert that HSD/hEDS is often under-recognized and poorly managed.[7,8]

Joint hypermobility is a body structure/function impairment, not a diagnosis; hypermobility can be localized to individual joints, limited to peripheral joints, or generalized.[2] Although genetic abnormalities have been identified for other forms of EDS, no specific genetic abnormality has been associated with HSD/hEDS. The pathophysiology of HSD/hEDS remains unclear and is likely to be multifactorial. Several defects in the connective tissue proteins have been found, including Type I, III and V collagen and tenascin X.[9] While joint hypermobility is often the most visible abnormality, HSD/hEDS affects connective tissue in many body systems, causing widespread signs and symptoms involving most body systems (see Tab. 1).[4,10-12] Some have proposed that HSD/hEDS is due to abnormal connective tissue assembly resulting from chronic mast cell activation.[13] It is important to remember that joint hypermobility may exist for reasons other than ligamentous laxity, such as myopathies, neurological or skeletal disorders; Marfan syndrome, Loeys-Dietz syndrome and Beals syndrome are a few examples.[1,2]

The wide range of presentations and problems in this population triggered the 2017 creation of The International Consortium on Ehlers-Danlos Syndrome & Related Disorders to consolidate knowledge, research and clinical needs in EDS. The American Journal of Medical Genetics ran series of 18 articles addressing the wide range of presenting complaints and comorbidities, and provides the foundation for the current Perspective; full text of these articles is available at https://www.ehlers-danlos.com/2017-eds-international-classification/.

The purpose of the current Perspective article is to improve the ability of physical therapists to 1) recognize HSD/hEDS and apply the diagnostic criteria for hEDS, 2) understand the impact of multi-system involvement on function, disability, and PT intervention, and 3) apply evidence-based practice principles integrating research, clinical expertise and patient preference to effectively manage these complex patients. Two case scenarios, one adult and one pediatric, are provided in

the eAppendix (available at https://academic.oup.com/ptj) to help readers visualize information presented in the article.

Clinical Presentation

Patients with HSD/hEDS may present with a wide range of signs and symptoms (see Tab. 1).[4,10,12] All individuals with HSD/hEDS have hypermobile joints, either currently or historically. Additional signs and symptoms vary significantly among individuals, with some people affected mostly by pain, others by fatigue, yet others by symptoms such as dysautonomia, coordination deficits, etc. Although long-term longitudinal studies are lacking, cross-sectional studies suggest that the presentation of HSD/hEDS tends to change over the life-span. Childhood and adolescence may be characterized by delayed motor development, poor coordination, fatigue, gastrointestinal problems and intermittent pain often associated with dislocations or sprains. The second and third decades of life tend to be dominated by recurrent muscle, joint, tendon and peripheral neurogenic pain, sleep disorders, and urogenital problems. Later adulthood tends to be associated with widespread chronic pain (including fibromyalgia), disabling fatigue, central sensitization and multiple visceral problems.[14] Each person's progression will be different; however, a 3-year prospective study in children found that those with multi-system involvement, high initial pain and fatigue, and poor postural control had a worse prognosis[15]; this suggests that there may be different phenotypes within the HSD/hEDS population.

Severity and complexity can vary, in HSD/hEDS, from mild/simple cases with only a few mild complaints to severe/complex cases who may be completely disabled by hypermobility-related complaints.[15,16] Some people with HSD/hEDS experience flares, particularly after periods of over-

activity or inactivity due to injury, illness, or stressful life events. Any of these triggers can exacerbate muscle weakness due to pain or deconditioning, which further increases joint instability.[17]

The clinical presentation of HSD/hEDS is further complicated by the common triad[18] of HSD/hEDS with Postural Orthostatic Tachycardia Syndrome (POTS) and Mast Cell Activation Syndrome (MCAS), whose symptoms are listed in Table 1.[18-21] The exact reason for frequent POTS in HSD/hEDS is not clear, but may be due to both peripheral vascular pooling in hyperelastic vascular structures and abnormal sympathetic activity.[19,22] The link between MCAS and HSD/hEDS is also unclear, but is proposed to be through an excess of chymase-positive mast cells affecting connective tissue.[13,18]

Examination of Patients with Hypermobility Spectrum Disorder

The history should use a biopsychosocial approach and address the multisystem involvement typical of HSD/hEDS. Often patients are unaware that non-musculoskeletal symptoms are associated with HSD/hEDS and might not offer this information unless asked.[23] The International Classification of Function (ICF) model provides an effective way to integrate body structure/function impairments with functional restrictions, personal and environmental factors.[24] Disability, in HSD/hEDS, may be due to pain, fatigue, or psychological distress,[25] so each of these domains should be probed. Childhood symptoms, such as clumsiness or developmental delay, are also relevant.

Some components of the hEDS diagnostic criteria are assessed through the history. Formal diagnosis of a 1st degree relative with hEDS is one of the diagnostic criteria. History of hernias,

organ prolapse, recurrent non-traumatic dislocations, mitral valve prolapse and aortic dilatation are considered characteristics of a systemic connective tissue disorder (see Fig. 1).[10]

The history should also include questions about contributing factors, common postures or provocative activities, especially when there is no traumatic onset; because of tissue fragility, aggravating factors may be more subtle than for non-HSD/hEDS patients. The interview should also ask about periods of inactivity due to illness or life events, as these may also trigger episodes of increased symptoms.

At this time, the Bristol Impact of Hypermobility questionnaire is the only outcome measure validated specifically for JHS but it has not yet been validated for HSD/hEDS or in children under the age of 18 years. It asks about locations of pain in the past 7 days, and an additional 55 questions addressing the following areas: severity and impact of pain, joint instability, functional limitation, pain with activity, self-efficacy, and life interference in the past 7 days.[26] Test-retest reliability intraclass correlation coefficient (ICC) is 0.923 (95% CI 0.900-0.940) and the minimum detectible change is 42 points (19%).[27] Cut-off scores for levels of disability have not yet bet published. The Pediatric Quality of Life Measure (PedsQL) is a useful generic outcome measure for children as it covers physical function, emotional, social and school domains.[28]

The physical exam includes items in the diagnostic criteria for hEDS (See Fig. 1 for a diagnostic checklist, available at www.ehlers-danlos.com). The Beighton score assesses hypermobility at the elbows, knees, thumbs, 5th MCP and trunk, as shown in Figure 1. The required number of hypermobile joints varies with age: at least 6/9 for pre-pubertal children, at least 5/9 for adolescents-50 years, and at least 4/9 for individuals over 50 years old. Individuals who are 1 point

below the threshold may score 1 additional point by answering Yes to at least 2 questions in the Five-Point Questionnaire (see Fig. 1), which asks about historical hypermobility[10]

The diagnostic criterion for a systemic connective tissue disorder include: soft velvety skin; mild skin hyperextensibility at the volar forearm (1.5 cm); unexplained stretch marks; piezogenic papules in the heel (nodules visible with weight bearing); atrophic scarring. Other connective tissue features include umbilical, inguinal or abdominal hernias and pelvic floor, rectal or uterine prolapse. Marfanoid signs of arachnodactyly (tested using arms-span to height and the Steinberg or Walker signs), and high narrow palate can also be assessed.

Further physical examination should be based on the patient's complaints, to identify functional limitations, symptomatic tissues, and factors contributing to those symptomatic tissues (see Tab. 1).[12,29] Functional limitations can be assessed using standard outcome measures based on the patient's level of function, which can range from high level athlete to bed-bound.

Therapists should be particularly attentive to quality of movement and motor control, not just outcome and function. Some studies suggest that people with HSD/hEDS have proprioceptive deficits, at least in the lower extremities,[30,31] while other studies suggest decreased precision of movement correlating to the Beighton score.[32,33] Balance[34] and postural control[35] also appear to be compromised, at least in children.

Since many patients with HSD/hEDS complain of fatigue and other POTS-related symptoms, a Stand Test can substitute for the formal tilt-table test: take the patient's heart rate after 5 minutes of

resting supine, then at 2, 5, and 10 minutes after quickly standing still (without fidgeting); it is helpful to monitor blood pressure to rule out orthostatic hypotension.[36] If doing a Stand Test, position the patient's back against a wall and be prepared for possible episodes of syncope.

Younger children with HSD/hEDS may present to PT due to pain, fatigue, or developmental delay due to poor motor control, proprioception, and strength.[37-40] Examination should include sitting and standing posture, where children may hang on ligaments (eg, genu recurvatum, pes planus) and poor stabilization (eg, winging scapulae or excessive lordosis); upper extremity weight-bearing tests, such as quadruped, may demonstrate hyperextension of elbows or wrists. Functional strength and dynamic control in midrange can be observed during movements such as wall squats, heel raises, single leg stand, bridging and quadruped reaching. Standardized developmental assessment might not reflect poor quality of motion seen in children with HSD/HEDS.[41] Gait abnormalities are also common, but are variable between and within individuals.[39] Children tend to have decreased knee flexion in swing and excessive extension in stance; both children and adults tend to have decreased lateral joint stability.[42] The examination should include some aspect of endurance testing, as fatigue can exacerbate instability and poor motor control.[43] As with adults, the pediatric interview should also ask about complaints in other systems, as multi-system involvement has been shown to predict more disablement.[15]

Evaluation, Diagnosis, and Prognosis

Figure 2 shows a flow chart guide for management of patients suspected of HSD/hEDS[2,4,10,29] Current and historical hypermobility should be assessed in patients presenting with complaints typical of HSD/hEDS. Genetic testing is only appropriate if one of the other forms of EDS is suspected. The second most common form of EDS is classical EDS, which has more significant skin

involvement. Even though vascular EDS is not common, physical therapists should consider it due to life-threatening risk of aortic or organ rupture; patients with vascular EDS typically have translucent skin with prominent veins, easy bruising, and a characteristic facial appearance with prominent eyes.[10]

The 2017 diagnostic criteria for hEDS (Fig. 1) have 3 criteria that must all be met: 1) generalized joint hypermobility, 2) systemic manifestations of a connective tissue disorder (and 3) exclusion of other conditions. Criterion 1, generalized hypermobility, has been described above. Criterion 2 requires that at least 2 of 3 sub-categories be met (systemic connective tissue involvement, 1st degree family history, and musculoskeletal pain or dislocations).[10] Criterion 3 is exclusion of other conditions associated with hypermobility (see Fig. 2) and may require referral for further medical testing. The restrictive diagnostic criteria for hypermobile Ehlers Danlos Syndrome (hEDS), compared to JHS and EDS-HT, is an attempt to identify a more homogeneous population in an effort to identify a specific genetic etiology.[10] Many people who used to meet the diagnostic criteria for JHS or EDS-HT do not meet the criteria for hEDS, and are now included in the category of HSD, which is the presence of generalized laxity and a few of the characteristics of hEDS but not enough to meet the stricter criteria.[1,2]

It is important to identify relevant comorbidities. The diagnostic criteria for POTS are heart rate increase of ≥30 bpm within 10 minutes of a standing or tilt-table test in the absence of orthostatic hypotension (no drop of >20 mm Hg systolic blood pressure); children must demonstrate heart rate increase of ≥40 bpm. Patients should have no other reason for their tachycardia, such as prolonged bed rest, conditions or medications affecting autonomic regulation.[19,20] The presence of POTS affects PT interventions, as patients may have poor exercise tolerance, especially to upright activities; post-operative patients may be particularly vulnerable to syncope episodes.

Diagnosis of MCAS is beyond the scope of this article, and readers are referred to other sources for more information[18,44] Fibromyalgia is a common comorbidity of HSD/hEDS and may be misdiagnosed when the actual diagnosis is HSD/hEDS[12]; fibromyalgia should be assessed using the 2016 American College of Rheumatology 2016 diagnostic criteria, not tender points.[45] One longitudinal study suggests that multi-system involvement is associated with greater disability and worse prognosis.[15] Consequently, other system involvement may justify referral to gastroenterologists, nutritionists/dieticians, immunologists, psychologists, etc.

Once identification of HSD/hEDS and possible comorbidities has been completed, evaluation needs to prioritize the patient's problems and determine whether this is an active, stable patient with an acute injury or a deconditioned, unstable patient. Similarly, differentiation between mild/simple cases and severe/complex cases facilitates a tiered approach to management.[15,16] For example, a 'simple' patient might present with a recent history of patellofemoral pain due to pes planus and muscle length-strength imbalances around the hip and knee. A 'complex' patient may present with widespread pain of long duration, multiple system involvement, multiple comorbidities, and significant psychosocial distress. Although pain, fatigue, multi-system involvement and psychological distress all contribute to disability, fatigue and distress are more highly correlated with disability than pain.[15,16] Consequently, a biopsychosocial approach should address multiple issues in these patients.

Children with HSD/hEDS frequently have poorer quality of life than non-hypermobile peers. Factors contributing to quality of life deficits in children include pain, fatigue, stress incontinence and gastrointestinal disturbance.[46] Early studies suggest that 75% of patients develop symptoms

prior to age 15.[47] Hypermobile adolescents are twice as likely to develop musculoskeletal problems than non-hypermobile peers. Overweight teens are 12 times as likely to experience pain.[48]

In addition to identifying symptomatic tissues, the PT needs to identify factors contributing to symptoms. Figure 3 lists common contributing factors that should be identified and addressed. Psychosocial factors can significantly impact pain and disability.[16] It is also important to determine the type of pain, as inflammatory and mechanical nociception should be managed differently from peripheral neuropathic pain, which is different from peripheral or central sensitization.[29] A thorough investigation into patients' past medical history and understanding the severity of their current and potential added complications from other medical conditions and how they interact with their general health and fitness level will help create a plan of care with a reasonable timeline and goals.

Treatment Strategies for the HSD/hEDS Population

There is limited research evidence for treatment of HSD/hEDS. However, existing evidence and expert opinion support the belief that physical therapy is essential for individuals with HSD/hEDS and, if implemented correctly, can help decrease pain and improve endurance, outlook on the impact of the disorder, and quality of life in those with HSD/hEDS.[49] Success in physical therapy has been linked to a combination of a diagnosis of the joint hypermobility disorder prior to the start of therapy and a therapist who is knowledgeable in regard to effective treatment strategies for such patients.[50,51] The approach in physical therapy should be multifactorial and address all of the patient's needs. This may include: patient and caregiver education; exercises the patient can consistently tolerate; pain, fatigue and stress management; self-management techniques; splinting or bracing recommendations; cognitive behavioral strategies; and referral to other providers as

appropriate. Figure 2 shows the manifestations of HSD/hEDS that can often be managed with physical therapy and those that typically require referral to other providers.

As noted, above, patients may present as simple/acute, intermediate, or complex/chronic. In general, simple/acute patients may benefit from typical rehabilitation activities such as neuromuscular re-education, therapeutic exercise, manual therapy, and modalities; patient education about injury prevention, body mechanics and joint protection are important to minimize future injury. Intermediate patients may also require additional guidance regarding activity modification and pacing. Complex/Chronic patients may require multidisciplinary care, chronic pain management and cognitive behavioral approaches with an emphasis on teaching self-management skills. While creating a physical therapy plan of care for this group of patients may seem daunting, the process is similar to the rest of the general population. Begin by identifying the primary reason the patient is seeking treatment: managing an acute or chronic problematic area, general deconditioning, or education purposes only.

Effective communication and education are critical because these are life-long disorders and self-management is crucial for patients of all ages.[50,51] Patients who fully understand their condition, triggers and reactions, and self-care strategies can more-effectively manage pain and disability, and more efficiently recover from a flare-up or injury.[50,51] Furthermore, patients value physical therapists as partners who listen and collaborate.[51]

Patients and parents/carers should know strategies for joint protection and avoiding activities and positions that place excessive stress on joints and stabilizing muscles. Understanding of body mechanics and ergonomics can minimize stress to the body. Although research is inconclusive,

experts suggest that external joint support such as braces and splints can help protect both large and small joints for functional or recreational activities; adaptive utensils and tool modifications may decrease stress on hand joints. Patients should know when and how to use such assistive devices.[24,30] One of the benefits of bracing may be through providing additional proprioceptive input through enhancing cutaneous sensory input; compression clothing, taping and orthotics may enhance proprioception.[52]

Experts recommend gradually progressed exercises guided by motor learning theory to ensure quality movement.[50,53] Augmented or external feedback may be particularly helpful in this population due to decreased proprioception,[54] and patients report that a 'hands on' approach to help guide and aid learning is beneficial.[51] Proprioceptive training can be beneficial both for improving movement precision and for decreasing kinesiophobia often found in this population; movement training can help prevent fear avoidance strategies that can amplify functional impairments.[55,56] Studies suggest that proprioceptive training should include the hypermobile range, rather than having patients avoid those ranges.[57]

Both general strengthening and targeted strengthening of injured joints are beneficial in reducing pain. Joint stability can be addressed through postural awareness, proper body mechanics, muscle strengthening and motor control training, and consistent physical activity to improve overall physical fitness.[31,49,58] Muscle mass in those with hEDS, while comparable in size to the general unaffected population, demonstrates decreased strength, strength endurance, and functional capacity.[59] Maintaining muscle strength to reinforce joint stability can reduce chronic widespread joint pain or specific deficient joints that are problematic or injured.[50,58] Spinal stabilization exercises can decrease pain and improve function.[60]

When strengthening, progression should be slow to avoid irritating unstable joints and surrounding easy-to-irritate muscles and tendons, which respond differently to muscle activation than the normal population. This impaired firing pattern may be related to the altered connective tissue found in the extracellular matrix of muscle fiber impacting force transmission of the contraction, along with increased elasticity of the muscle tendon complex to work against during muscle firing.[59,61]

Consistent physical activity that is appropriate for the patient is crucial for long-term management of both musculoskeletal and systemic symptoms. Weight management is important, especially for young people.[48] The physical activity chosen for the individual must be appropriate and safe for the individual. For example, many patients do not tolerate high-impact activities. However imposed restrictions may not be as necessary for the hypermobile patients as once thought, as a number of studies suggest that injury rate during activity may be no greater for individuals with GJH, or that some joints may be at risk while others appear not to be.[62-64]

Patients with HSD/hEDS can have tight muscles pulling on lax joints, which might cause greater imbalance in hypermobile patients compared to individuals with normal joint flexibility. While stretching joints is commonly discouraged in patients with hypermobility, focused stretching can be appropriate if needed to address muscle imbalances with the local joint maintained in a stable position. Physical Therapists should avoid encouraging overpressure on joints into open packed positions or providing any form of stress to a hypermobile joint.

Aquatic therapy is often beneficial in the HSD/hEDS population.[51] As with all exercise, therapists should pay close attention to the patient's form and response to the exercises. While joint compression forces are decreased in water, resistance caused by drag forces in water can strain muscles, tendons and ligaments required to stabilize the joints. Patients with POTS may benefit from improve venous return produced by hydrostatic pressure, but may have poor tolerance to prolonged time in cooler water and may require warmer, therapeutic pool temperatures. Patients with MCAS may be irritated by the chemicals in the water.

Fatigue can be addressed through patient education and exercise. Patients should be educated about sleep hygiene, relaxation and stress management, pacing and prioritizing. A gradually progressed exercise program can address deconditioning, but may need to start at very low levels to avoid 'boom and bust' cycles.[65] Muscle strengthening can also decrease fatigue.[66] For patients with POTS, lifestyle changes and POTS-specific exercises are helpful.[19,67]

POTS and other autonomic dysfunctions can create fluctuating exercise intolerance, and in more severe cases, postural intolerance that can be triggered by changes in vertical position that can occur frequently with exercise. The Dallas protocol, available online from the Children's Hospital of Philadelphia, (http://www.dysautonomiainternational.org/pdf/CHOP_Modified_Dallas_POTS_Exercise_Program.pdf) recommends a slow, progressive program beginning with horizontal exercises and lower extremity and core strengthening to facilitate venous return, with an 8-month progression of cardiovascular training toward upright exercise. Patients need to be aware that recovery from POTS requires many months of exercise. This approach is supported by the growing research evidence base in adults[68] and best practice guidelines for adolescents.[67]

Recognition of the systemic issues commonly associated with HSD/hEDS by the physical therapist is instrumental in promoting the best possible treatment outcomes. For example, MCAS issues in physical therapy can range from skin reactions to adhesives and slow healing of wounds to systemic and local inflammatory reactions and severe fatigue, all of which can vary daily in intensity.[18] Patients may also be affected by fragile skin, anxiety, cognitive fatigue, gastro-intestinal problems, incontinence and gynecological issues[4]; the physical therapist may need to educate patients and families, refer to other professionals, or accommodate these issues within the physical therapy plan of care.

Pain management is often very difficult for these patients and flare-ups of uncontrolled pain usually precipitates physical therapy visits. Patients with HSD/hEDS frequently report insufficient pain control even when on multiple analgesics.[69] Pain education helps patients understand their pain and how to ultimately self-manage appropriately in a style that works for them. With children, it important that parents /carers understand how to parent a child in pain. For example, how to use ice, heat and braces. Cognitive behavioral approaches targeting both parents and children are helpful in managing pain.[70] Learning proper body mechanics and slow and steady progression of activities can prevent overuse injuries or an inflammatory response. Cognitive behavioral approaches such as relaxation, coping skills, sleep hygiene and rest can reduce symptoms.[56] There is no current evidence regarding modalities for reducing pain in this population, but modalities may be helpful.[23] Pharmacological management of pain in HSD/hEDS is beyond the scope of this article; readers are referred to recent reviews[12,29] for additional information.

Although there is limited research, experts suggest that manual therapy techniques, such as soft tissue mobilization, can be helpful in reducing pain.[24] A recent case report demonstrates how manual therapy such as trigger point release and focused joint mobilization might be integrated into a comprehensive program for a patient with HSD/hEDS.[71] Joint mobilizations are typically avoided unless there are compensatory issues restricting certain areas of the capsule that must be addressed to restore proper muscle balance and alignment. Any manual therapy must be implemented carefully due to fragile tissues.[23]

Because patients with HSD/hEDS have slow and poor tissue healing, surgical interventions should be avoided if conservative care might be effective.[4,72,73] One study found that only 33.9% of surgical interventions for people with HMS were considered successful, compared to 63.4% success with physical therapy.[69] When surgery is appropriate, recommendations include minimizing surgical incision size and tissue traction, avoiding skin clips, supplementing sutures with steristrips and leaving sutures in place for longer than normal.[74]

In summary, patients with HSD/hEDS are likely to present to physical therapy with a variety of complaints involving multiple body systems beyond just musculoskeletal. The flow chart in figure 2 proposes a patient management approach for patients suspected of having HSD/hEDS. Treatment provided by physical therapists knowledgeable about this condition is key to managing it effectively. Patient and family education is critical so patients can actively engage in self-management and injury prevention. Tissue fragility may decrease patient tolerance to interventions such as exercise or manual therapy, and patients are likely to progress more slowly than non-hypermobile patients. Since research is just beginning to provide evidence regarding optimal interventions for this condition, therapists will need to integrate existing research with clinician

expertise and patient preference to maximize the benefit for each individual patient. Adult and pediatric case scenarios in the eAppendix illustrate the concepts presented in this article.

Author Contributions

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Disclosures

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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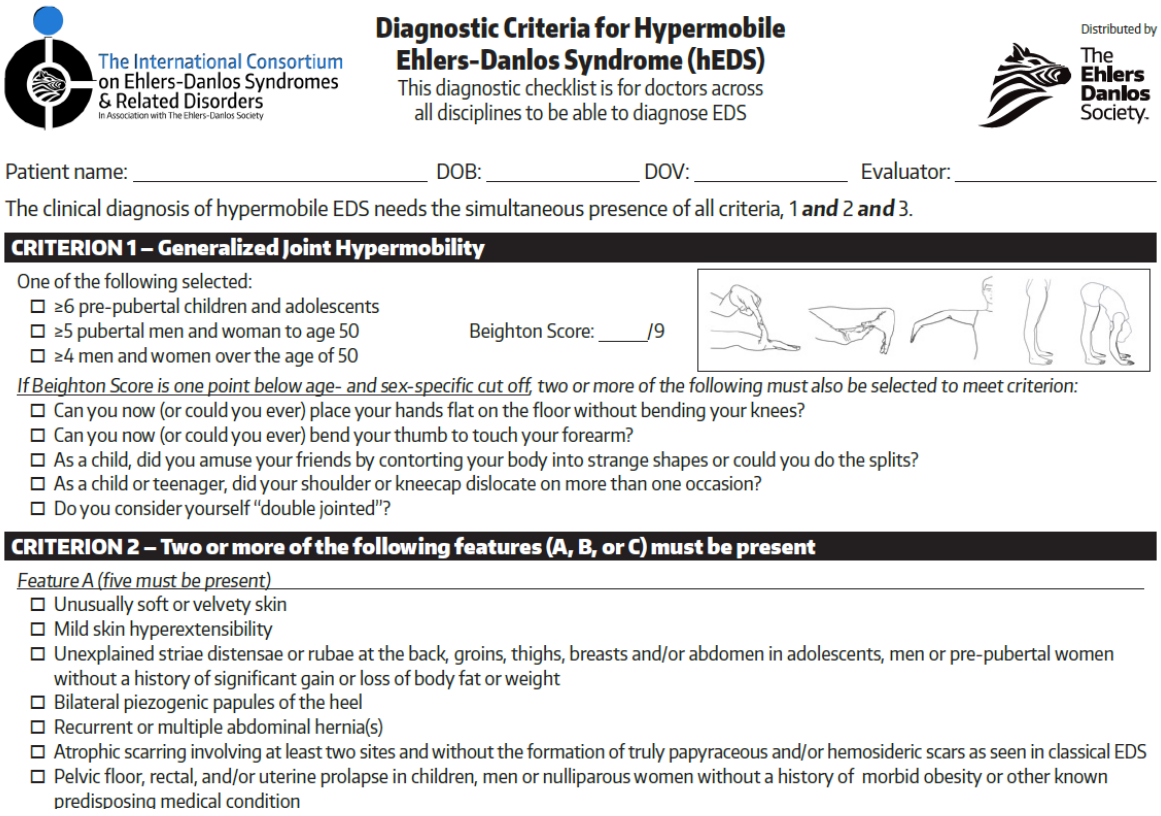
Table 1: Common Signs and Symptoms Associated with Hypermobility Spectrum Disorder and Hypermobile Ehlers-Danlos Syndrome.[4,10,12]

Systems Affected	Health Issues
Bones and joints	● Frequent sprains, subluxations, and dislocations ● Chronic joint pain, osteoarthritis ● Scoliosis ● Decreased bone density, increased fracture rate (controversial)
Soft tissues	● Tendinitis, bursitis, synovitis, tenosynovitis, fasciitis, or tendon ruptures ● Trigger points, muscle spasm, muscle strain
Autonomic	● Dysautonomia with orthostatic hypotension and/or postural orthostatic tachycardia syndrome (POTS) presenting with: tachycardia, pre-syncope/syncope, anxiety, chronic fatigue, sleep disorder, exercise intolerance, dependent edema, purpling skin, temperature dysregulation, "brain fog," and trouble concentrating ● Raynaud syndrome
Cardiovascular	● Varicose veins ● Mitral valve prolapse or aortic dilatation (not common)
Neurological	● Motor delay (in children) ● Proprioceptive and motor control deficits leading to clumsiness, frequent falls, trips, or bumping into things ● Fibromyalgia/central sensitization, hyperalgesia ● Headaches, migraines, dizziness ● Paresthesias and nerve compression disorders ● Restless leg syndrome
Cognitive	● Anxiety and panic disorder

	• Memory or concentration problems • Depression
Gastrointestinal	• Irritable bowel syndrome, constipation or diarrhea, bloating, abdominal pain, gastroparesis, food sensitivities • Gastroesophageal reflux, chronic gastritis, heartburn • Prolapsed rectum • Hernias (all types)
Dermatologic	• Hyperextensible skin • Slow healing or scarring, poor wound healing • Easy bruising
Urogenital	• Urinary incontinence • Prolapsed bladder or uterus • Urinary tract infections • Dysmenorrhea, endometriosis, vulvodynia, pelvic pain, painful intercourse
Immune	• Mast cell activation syndrome (MCAS): hives, pruritis, flushing, chemical and environmental sensitivities, medication and food sensitivities, fatigue, trouble concentrating, migratory pain, excessive inflammatory response, trouble concentrating, anxiety
Non-system	• Insomnia, sleep disturbance, and debilitating chronic fatigue

Figure Legend



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

Figure 1: Diagnostic criteria for hypermobile Ehlers-Danlos Syndrome (hEDS).[10] This form is available at www.ehlers-danlos.com. Hypermobility Spectrum Disorder (HSD) is diagnosed when patients have joint hypermobility and some of the other presenting signs and symptoms, but do not meet the strict criteria for hEDS.[1,2] (Reprinted with permission from the Ehlers-Danlos Society).

CTD = connective tissue disorder.

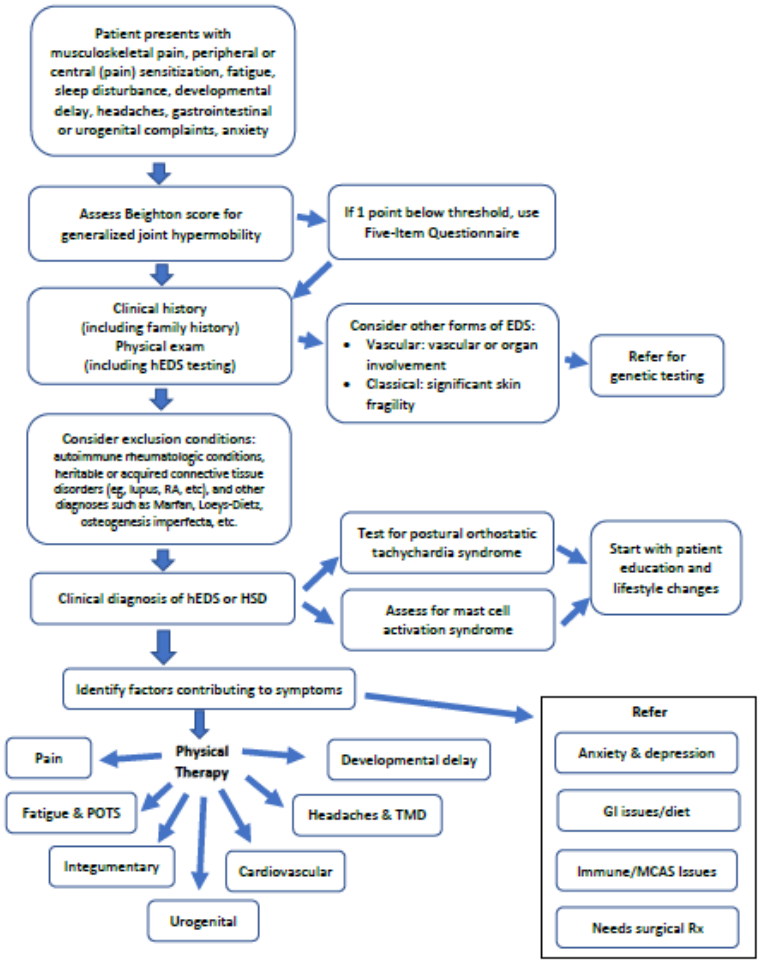


Figure 2. Flow chart summarizing diagnostic and management approach to hypermobility spectrum disorders. Patients may initially present with a variety of complaints. Once HSD/hEDS is suspected, diagnostic criteria for hEDS are assessed. Patients suspected of other forms of EDS may need further testing, including genetic testing, and testing for other exclusionary conditions may also be indicated. Patients suspected of HSD/hEDS should be assessed for POTS and MCAS, as these form a common triad. Physical therapy management of patients with HSD/hEDS starts with prioritization of the most significant complaints and may require referral for other system involvement. Flow chart adapted from multiple sources.[2,4,10,29]

EDS = Ehlers Danlos Syndrome; hEDS = hypermobile Ehlers Danlos Syndrome; HSD = Hypermobility Spectrum Disorder; MCAS = mast cell activation syndrome; POTS = postural orthostatic tachycardia syndrome; RA = rheumatoid arthritis; TMD = temporomandibular disorder.

1) Poor posture or gravitational forces placing excessive stress on joints or muscles
2) Body mechanics or positions stretching or stressing joints
3) Imbalance between loose joints and tight muscles
4) Poor proprioception or motor control
5) Myofascial trigger points caused by muscle overuse
6) Central sensitization

Figure 3. Common reasons for pain and instability.[12,29]