Orthopedic Physical Therapy Management of Joint Hypermobility Syndrome

Emma Shirley

The University of North Carolina at Chapel Hill

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Joint hypermobility syndrome (JHS) is a relatively common phenomena that exists on a spectrum of excess joint mobility. A joint's stability is the sum of its ligaments, muscles, tendons, and joint capsule. When any of these important stabilizing structures becomes deficient, joint hypermobility results. Joint hypermobility can be technically defined as excessive motion in the normal plane of a joint.[3] It can be limited to one or a few joints, or be as widespread as to affect the majority of all joints in the body. The term "generalized joint hypermobility" (GJH) is used to describe joint hypermobility when present in multiple joints. GJH can be present in any number of peripheral joints and/or the axial skeleton.[3] GJH can vary widely amongst individuals. People with GJH can present with hypermobile joints without developing symptoms or complications.[3,4,10] However, GJH can become symptomatic, creating debilitating symptoms, complications, and comorbidities. The spectrum of GJH at its best begins as asymptomatic hypermobility in a small number of joints, ranging to symptomatic hypermobility that has been known historically under diagnoses such as Joint Hypermobility Syndrome or Ehlers-Danlos Syndrome.[7]

Ehlers-Danlos Syndrome (EDS) is an umbrella term referring to thirteen genetic subtypes of a heritable connective tissue disorder.[1,3,4,5] Each subtype is clinically and genetically heterogenous from one another and present with a wide variety of symptoms. However, all subtypes of EDS are characterized by GJH, skin hyperextensibility, and musculoskeletal complications without systemic inflammatory joint disease; GJH is frequently cited as the most prominent feature of EDS.[1,3,4] The hypermobile type of EDS, or hEDS, is the only subtype of EDS that does not have a confirmed specific genetic abnormality.[12] As such, hEDS is diagnosed via rigorous

diagnostic criteria (see Appendix A.)[3] It requires characteristics such as GJH, presentation of abnormally soft, fragile skin, a family history of EDS, and musculoskeletal complications or pain.[3,4]

Another common diagnosis of symptomatic GJH is benign joint hypermobility syndrome (BJHS). It may also be referred to as hypermobility spectrum disorder (HSD). In the past, BJHS/HSD was seen as a separate diagnosis from hEDS. However, recently, researchers have recognized that, clinically, BJHS/HSD and hEDS are indistinguishable.[7] BJHS/HSD and hEDS are identical in potential clinical presentation.[3,5,7] Both can manifest as "joint subluxations/dislocations, periarticular pain, chronic diffuse pain, headaches, fatigue, postural dizziness, and/or gastrointestinal manifestations."[3] Historically, hEDS was primarily diagnosed in children, while BJHS/HSD was the chief diagnosis for adults.[3,4] Currently in the clinic and in research, BJHS/HSD and hEDS are seen as the same disease.[3,4,5,7,8]

GJH is also a characteristic of other heritable connective tissue disorders. These include Loeys-Dietz syndrome, Marfan syndrome, bone dysplasias, osteogenesis imperfecta, and achondroplasia.[3,4,7,9] Neurological disorders or other genetic conditions, including Noonan syndrome and fragile X syndrome, characterized by low muscle tone may also present with GJH due to the effects of low tone on joint dynamics.[3] For the purposes of this paper, JHS will refer to BJHS/EDS and presentation of any symptomatic GJH.

The exact pathophysiology of GJH and its symptom form, JHS, is currently unknown. There are multiple mechanisms suspected. Overall, JHS is a "multifactorial condition resulting from a combination of environmental factors… and multiple genetic

factors, each contributing a small amount to the total phenotype."[3] It is thought that JHS may be in part due to defects in connective tissue proteins; this may include type I, III, and V collagen and/or tenascin X. There may also be abnormal tissue assembly secondary to chronic mast cell activation.[7] It is also thought that pubertal hormones affect JHS. Women tend to experience an increase in mobility during puberty, while men tend to experience a decrease in mobility during puberty. In this way, it can be seen that pubertal hormones may play a role in JHS.[3]

JHS's complexity, its variation in presentation, and the general lack of healthcare practitioner knowledge about JHS causes it to be frequently over-looked and misdiagnosed.[5,8] Diagnosis of JHS mostly relies on the Beighton scoring system. The Beighton consists of a series of movements to examine global joint hypermobility status. It is advantageous due to the limited number of joints examined, its quickness, the ease to administer it in-clinic, and its good inter-rater reliability. However, there is debate regarding the score threshold for hypermobility, especially due to the high variability in joint mobility across ages, sex, occupation, and exposures to environmental factors.[3]

GJH, with or without becoming symptomatic, is estimated to be present in as little as 2% to as high as 57% of the population.[3] Although healthcare practitioner knowledge and awareness of JHS is lacking, JHS is actually very common. JHS is likely more prevalent than is currently recognized due to the aforementioned diagnostic difficulties.[9,11,12] It is thought that JHS is "the most common inherited connective tissue disorder," even more prevalent than rheumatoid arthritis.[7] It more commonly occurs in females than males.[1-4] It is thought to be present in approximately 5% of all women and less than 1% of all men.[1] It is more likely to present in those of Asian and African

descent.[4] JHS is highly prevalent in female athletes, secondary to the advantageous nature of increased range for many sports, including gymnastics, dance, and swimming. It is estimated that 15-17.9% of adolescent and college-age female athletes have JHS.[9] In a retrospective study by Bronner & Bauer, a cohort of 180 total dancers with injury during their time at a Bachelor's in Fine Arts program were followed. Using the Beighton scale, it was found that "38% of included dancers were hypermobile using $\geq$ 5 cutoff scores, while 44% classified as hypermobile using $\geq$ 4 cutoff scores."[6] It was found that dancers had a much higher prevalence of GJH than the average population, even with a more rigorous cutoff.[6] Due to its high prevalence, it is vital that health care practitioners, such as orthopedic physical therapists, are knowledgeable about JHS. The following will describe JHS clinical presentation and orthopedic physical therapy management for JHS.

Chronic joint pain is widely seen as the primary complication of JHS. It is one of the top complaints for those diagnosed with JHS.[3] It is estimated that 55% of children diagnosed with JHS complain of pain.[1] It is thought that those with JHS experience chronic pain as a result of the excessive movement at joints. This causes increased stress on joint surfaces, ligaments, and surrounding structures, resulting in pain.[1] Another source of pain for those with JHS may be myofascial. Hypermobile joints depend disproportionately on musculotendinous function for stability due the deficiency of primary stabilizing structures. This may precipitate painful myofascial trigger points and muscular spasms.[3] Hypermobility can also alter musculoskeletal alignment. The biomechanics of a hypermobile joint are different from a typically mobile joint. The hypermobile joint may cause compensatory changes at other joints and structures, thus

magnifying cumulative strain and increasing experiences of pain. For example, a common manifestation of JHS is a flat foot, secondary to the collapse of the midfoot arch as a result of excessive laxity in the ligaments of the foot. This can result in pronation and heel valgus, precipitating gait disturbance and potentially resulting in knee and back pain.[3] Those with JHS experience pain most frequently in weight-bearing joints, including the ankle, knee, and hip, and in joints used for repetitive tasks, such as the shoulders, wrists, and hands.[3,10] Patients may also present with back pain, neck pain, and temporomandibular joint (TMJ) pain. Pain in the cervical spine and TMJ can manifest as frequent debilitating headaches.[3] In a study by Johannessen et al in 2016, it was found that those with JHS experienced greater pain intensity, lower shoulder function, and overall lower health-related quality of life versus age-matched controls. Those with JHS also were found to present with greater incidence of generalized pain, versus greater incidence of localized pain in controls. Also noted by Johannessen et al was the significant effect of pain on participation and activity in activities of daily living.[5] Chronic pain is often a lifelong issue for those with JHS. It can start in childhood and persist into adulthood.[10] It is suspected that, over time, JHS results in traumatic arthritis from accumulated wear-and-tear on hypermobile joints, further exacerbating chronic joint pain.[12] The chronic pain experienced by those with JHS may also progress with central sensitization. It is common to see those with JHS misdiagnosed or comorbidly diagnosed with pain-related disorders like fibromyalgia.[7]

Chronic fatigue is another primary complaint of those with JHS. It is theorized that due to joint pain and dysfunction, those with JHS avoid activity. This may cause deconditioning and decreased muscular endurance. These may contribute to physical

fatigue. Deconditioning has also been linked to greater pain experienced with and decreased participation in activities of daily living.[3] Chronic fatigue is also thought to be a result of chronic sleep disturbance, potentially secondary to chronic pain. Sleep can also be affected by "anxiety, depression, dysautonomia, pain, and medications," all of which can be associated with JHS and JHS management.[3]

Those with JHS endure joint instabilities and ligamentous laxity. In addition to already-deficient stabilizing structures, chronic pain may inhibit muscles surrounding the painful joint. As a result, there is reduced muscular control in an already lax joint.[1] Proprioception is also affected by JHS. Ligaments possess mechanoreceptors essential for protective reflexes; they trigger muscular action to protect joints from moving too far into extreme ranges that may result in damage. In JHS, joints are chronically lax. This laxity is thought to result in chronic, cumulative mechanoreceptor damage. It also may be that the deficient nature of connective tissue in those with JHS may also affect the integrity of ligamentous mechanoreceptors.[1] This may contribute to frequent joint subluxations and dislocations. Subluxations and dislocations additionally contribute to damage surrounding the tissue. It can be seen how this acts as a feedforward cycle of disability, where lax joints accumulate continuous damage over time.[3-5]

Dysautonomia and orthostasis are also associated with JHS, and particularly with forms of EDS. Dysautonomia is characterized by chronically low blood pressure and postural dizziness. Orthostasis is low blood pressure, particularly low diastolic blood pressure in the 50's or 60's. Orthostasis peaks in adolescence and young adulthood. The link between JHS and orthostasis is not particularly understood but the relationship

is well-documented. Those with JHS and orthostasis may be comorbidly diagnosed with orthostasis-related conditions such as postural orthostatic tachycardia syndrome (POTS), neutrally mediated hypotension, idiopathic supraventricular tachycardia, or orthostatic intolerance.[3] POTS has been strongly linked with JHS. It is also thought to be related to the manifestation of gastrointestinal issues. POTS itself is theorized to be a result of peripheral vascular pooling in hyperelastic vascular structures paired with abnormal sympathetic activity.[7]

JHS is frequently accompanied by functional gastrointestinal disorders, such as dysphagia, reflux, chronic abdominal pain, bloating, and diarrhea.[3,14] Gastrointestinal disorders can occur along the length of the entire gastrointestinal tract.[4] The abnormal quality of connective tissue in those with JHS is not limited to the musculoskeletal system and can also affect tissues of any body systems containing connective tissue. It is thought that in those with JHS, deficient connective tissue quality allows "increased visceral compliance that promotes hollow organ distension, and… changes in both pain thresholds and gut motility can contribute to various functional [gastrointestinal] complaints."[4] Dysautonomia is thought to be related. In a recent study, it was found that individuals with hiatal hernias and gastroesophageal reflux disease were "more likely to have abnormal elastin deposits depositions in their phrenoesophageal and gastrohepatic ligaments than those with [gastroesophageal reflux disease] alone."[4] Thus, it can be seen the integrity of an individual's connective tissue can be intricately related with gastrointestinal health.

The majority of treatment for JHS focuses on management of symptoms. Currently, there are "no disease-modifying therapies or investigational agents on the

horizon" for JHS.[4] It is difficult for patients with JHS to acquire proper treatment from health care professionals. In a focus group study of patients and health care professionals by Palmer et al in 2016, it was found that patients struggle to receive appropriate care from health care professionals. Patients cite not being believed, or that health care professionals doubted their diagnosis. Additionally, patients frequently complained of suffering a lengthy and complicated diagnosis process. Health care professionals in the focus group corroborated lack of knowledge regarding JHS. Overall, patients cited better experiences and higher quality of care when seeing health care professionals specializing in JHS.[11]

Physical therapy is frequently incorporated in management of JHS.[10,11] However, there is little actual scientific evidence to support its use.[11,12]

It is recommended that physical therapy practitioners use the biopsychosocial approach during patient evaluation due to the multisystem involvement and complex presentation of JHS.[7] The Bristol Impact of Hypermobility is currently the only objective measure specifically tailored to those with JHS. It is validated for use in patients with JHS older than 18 years. It is a self-report survey of 55 questions addressing "locations of pain in the past 7 days, severity and impact of pain, joint instability, functional limitation, pain with activity, self-efficacy, and life interference in the past 7 days."[7] It has a test-retest reliability intraclass correlation coefficient of 0.923 with a 95% confidence interval of 0.900 to 0.940. However, it has a relatively high minimal detectable change of 42 points, or 19%.[7] The Beighton score is also a quick and easy assessment tool to determine the magnitude of a patient's GJH.[1-7] The Stand test is an appropriate way to quickly screen for POTS in clinic. The patient's blood pressure and heart rate are

measured after 5 minutes of laying supine. Then the patient transitions to standing. Blood pressure and heart rate are again measured after 2, 5, and 10 minutes of quiet standing. The patient should stand against a wall and the therapist should be close by in anticipation of syncope.[4] It is important a physical therapist stay alert to signs of POTS secondary to its previously-discussed high prevalence with JHS.[3,4,7] A physical therapist should also pay attention to the quality of the patient's movement. This can include examining motor control, postural control, and any proprioception deficits.[1,2,7] A thorough postural assessment should be done with the patient in standing, sitting, and during gait, as well as any other activities in which the patient commonly participates.[1,2,3,7]

Exercise is an important part of JHS management. While the exact type, frequency, and dose most appropriate for those with JHS remains unclear, evidence generally supports exercise as safe and beneficial.[12] Deconditioning may occur with JHS as a result of the aforementioned cycle of chronic pain and fatigue. General exercise is an excellent tool to combat this. Consistent physical activity has been shown to be helpful for long-term management of musculoskeletal complaints, especially for weight management, for those with JHS.[7] Additionally, exercise may improve vascular tone in those with orthostasis, an aforementioned common comorbidity associated.[3] It can also improve deconditioning and mitigate fatigue.[7] The mode of activity chosen should primarily be safe for the patient; it is generally recommended those with JHS avoid contact sports and activities in which extreme ranges are frequently taxed. However, the activity must be of interest to and enjoyable for the patient.[14] Individuals with JHS may have a decreased maximal exercise capacity

compared to normal, so the selected activity should also be attainable in this aspect.[12] The physical therapist should promote physical fitness, exercise, and sport participation for those with JHS. A specific mode of activity frequently implemented by physical therapists is hydrotherapy and aquatic therapies. Hydrotherapy has been shown to be well-tolerated by those with JHS. Exercising in the pool can decrease overall joint compressive forces, while the drag of the water creates resistance on tissue structures. However, caution should be taken when implementing a pool program with those with JHS; individuals with comorbid POTS or autonomic dysfunction diagnoses may be unable to tolerate the water if it is not an appropriate temperature.[7]

In those with JHS, muscle weakness is a "common clinical finding" and is often accompanied by complaints of pain.[14] It is also thought that there is an impaired muscular firing pattern secondary to deficient connective tissue in the extracellular matrix of the muscle fiber, thus impacting the force transmission of muscular contraction.[7] Targeted strengthening of stabilizing musculature around hypermobile joints may increase joint stability and thus reduce pain.[1] Increasing muscle strength may "reinforce joint stability," thus decreasing joint pain.[7] Specifically, closed chain exercises may reduce strain on injured ligaments while enhancing proprioceptive feedback to the joint. Exercises should be gradually progressed to avoid irritating joint structures and tissues.[7] It is also thought that there is an impaired muscular firing pattern secondary to deficient connective tissue in the extracellular matrix of the muscle fiber, thus impacting the force transmission of muscular contraction. Muscle in those with JHS has also been found to demonstrate "decreased strength, strength endurance, and functional capacity" despite comparable muscle mass to the general population.[7] As such, strengthening

exercises should be progressed slowly, providing ample time for appropriate adaptation to stimuli. Progression should include motor control and motor learning theory principles. It is important when working with those with JHS to incorporate augmented, external feedback over internal feedback; individuals with JHS may have a decreased ability to detect and process internal feedback.[7]

Proprioceptive and kinesthetic training is beneficial for physical therapists to incorporate in interventions. Individuals with JHS often struggle with proprioception, which is suspected to be secondary to cumulative damage to mechanoreceptors over time. Good evidence exists supporting the use of proprioceptive training as a means to increase joint positional sense.[14] Coupled with proprioceptive difficulties may be kinesiophobia, or a fear of movement. Evidence also suggests that proprioceptive training may help alleviate kinesiophobia in those with JHS. Some evidence points toward benefits of training proprioception in the hypermobile range.[7] This is contrary to typical avoidance of hypermobile range; however, it may be beneficial for those with JHS to undergo supervised, controlled training in the hypermobile range to reduce kinesiophobia.[7]

Exercise is generally preferred over passive interventions like joint protection.[14] There is only limited evidence to support the use of joint protection braces and splints with those with JHS.[7,12] Bracing and orthotics may precipitate muscular atrophy and resultant weakness, which is counterintuitive to the general goal of increasing musculotendinous stability across hypermobile joints.[3] However, they can play appropriate roles for joint protection and support when implemented in conjunction with therapy. For example, braces may help increase confidence when working with an

individual with high kinesiophobia.[3] Additionally, braces may help proprioceptive input due to the cutaneous sensory stimulation provided by compressive garments.[7] Shoe orthotics are frequently used by those with JHS; the hypermobile foot may require features such as a strong heel counter for enhanced stability and support.[14] Those with JHS also can experience metacarpophalangeal and interphalangeal joint laxity. This can be supported via digital ring splints.[3] Occupational therapists can also help patients with adaptive utensils and tool modification to reduce stress on hypermobile or lax wrist and hand joints.[7] Hand splints can be appropriate if implemented to stabilize, but fashioned to still enable function.[14]

Physical therapists may implement pain management strategies to alleviate chronic pain commonly experienced with JHS.[3,7] Lax joints are frequently the site of myofascial trigger points and painful muscle spasms. In children, this is often mistaken for growing pains. Evidence supports relief may be found from incorporating modalities, such as heat and ice, at painful joints, particularly when paired with strengthening.[3,7] Manual therapy is also appropriate for trigger point relief.[3,7]

In addition to the aforementioned considerations for physical therapy intervention, there are several additional special considerations of which physical therapists should be aware. Individuals with JHS are a unique and complex patient population. They often have highly sensitive skin. Their skin is often described as ‘velvety’ and can easily bruise.[4] Skin breakdown occurs very easily and skin healing is much slower than is normal. Due to this slow tissue healing, it is important that physical therapists advocate for their patients with JHS to avoid surgical interventions as much as possible. If surgery is absolutely necessary, the surgical incision site should be

minimized. Tissue traction during surgery should be avoided. Additionally, skin-closure strips should be opted for over sutures. If sutures are used, they should be left in place for a longer period of time than normal, to provide ample time for sufficient tissue healing.[7] Any manual therapy interventions should be implemented with caution and exceptional gentleness.[3,7] Patients with JHS may also present with POTS, dysautonomia, or orthostasis diagnoses that reduce their exercise tolerance. It is essential to monitor the vitals of those with JHS during any physical activity.[3,4,7] Also frequently comorbid with JHS are psychiatric conditions. Most commonly, these present as panic disorders, agoraphobia, or simple phobias. Some evidence exists linking hEDS/JHS to anxiety and panic-related disorders, but the heterogeneity of JHS presentation and diagnosis makes drawing a clearly delineate relationship difficult.[8] Physical therapists should be vigilant and screen appropriately for mental health needs, and refer as needed.

While physical therapists are key health care providers to those with JHS, they exist as part of a diverse multidisciplinary team. Those with JHS have a wide assortment of needs best met by different disciplines. A retrospective cohort study from 2009 to 2015 analyzed the effectiveness of a multidisciplinary approach to treating pain in children with JHS. The approach included physical and occupational therapies, psychology, relaxation training, and medication management. It was found that this approach improved pain and physical and psychological functioning more so than usual care.[15] Psychology is frequently involved in treating those with JHS. As previously mentioned, JHS may have a relationship with mental health disorders such as panic and anxiety disorders.[8] Psychological approaches are also implemented for dealing with

pain sensitization. Evidence shows cognitive behavioral therapy is beneficial for treating pain sensitization and for management of chronic pain.[3,7] Patients with orthostasis and/or gastrointestinal complaints would likely benefit from seeing either or both a registered dietitian and gastroenterologist. Orthostasis may require careful sodium, electrolyte, and fluid intake monitoring. Gastrointestinal complaints may be intervened with special diets. Some gastrointestinal complaints require advanced imaging and diagnostic testing to ensure the patient receives appropriate care.[3,4] Some gastrointestinal complaints may benefit from pelvic floor physical therapy depending on the nature of the complaint.[3] Individuals with JHS may take a wide array of medications from multiple providers; a pharmacist is an excellent resource for medication management.[13]

JHS is a highly prevalent, but unfortunately underrecognized, condition that presents primarily as GJH. This presents as widespread joint instability and ligamentous laxities, potentially resulting in recurrent joint subluxations and dislocations.[3,5] This contributes to a cycle of recurrent, cumulative tissue damage, resulting in chronic pain and chronic fatigue.[1-3,5,7,10,12] JHS may also coincide with dysautonomia, orthostasis, gastrointestinal disorders, and psychiatric or mental health conditions.[3,4,7,14] Physical therapists should perform a comprehensive evaluation when seeing a patient with JHS, with special attention to postural control, proprioception deficits, and quality of movement.[1,2,7] Physical therapists can incorporate muscular strengthening, proprioceptive and kinesthetic training, and pain management interventions into their treatment plan for a patient with JHS.[1,3,7,14] However, physical therapists are only one part of a large multidisciplinary team of health care practitioners

involved in management of JHS. Patients may require psychology, gastroenterologist, pelvic floor specialist, and pharmacist referrals, amongst others.[3,4,8,7,13] Physical therapists should be vigilant to signs patients may need a referral to another provider. Overall, JHS is a common disorder in which physical therapists play an important role for its management. With the help of appropriate, skilled interventions by physical therapists and other members of the interdisciplinary health care team, individuals with JHS can lead happy, healthy, and fulfilled lives.

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APPENDIX A.

Box 1
The diagnostic criteria for the hypermobile type of Ehlers-Danlos syndrome

The clinical diagnosis of hEDS needs the simultaneous presence of criteria 1 and 2 and 3.

Criterion 1: GJH with positive Beighton score[a]

- ≥6 for prepubertal children
- ≥5 for pubertal persons up to the age of 50 years
- ≥4 for those more than 50 years

Criterion 2: 2 or more among the following features (A, B, and C) must be present

Feature A: 5 or more of the following systemic manifestations of a generalized connective tissue disorder

1. Unusually soft or velvety skin
2. Mild skin hyperextensibility, tested on the volar aspect of the forearm (not over extensor surfaces)
3. Unexplained stretch marks (unrelated to puberty or weight change)
4. Bilateral piezogenic papules of the heel
5. Recurrent or multiple abdominal hernias (eg, umbilical, inguinal, crural)
6. Atrophic scarring involving at least 2 sites
7. Pelvic floor, rectal, and/or uterine prolapse in the absence of pregnancy or morbid obesity
8. Dental crowding and high or narrow palate
9. Arachnodactyly, defined by 1 or both of (i) positive wrist sign (Steinberg sign) on both sides; (ii) positive thumb sign (Walker sign) on both sides
10. Arm span/height ratio ≥1.05
11. Mitral valve prolapse, based on strict echocardiographic criteria
12. Aortic root dilatation with Z-score greater than +2

Feature B: positive family history, defined as 1 or more first-degree relatives independently meeting the current diagnostic criteria for hEDS.

Feature C: at least 1 of the following musculoskeletal complications

1. At least 3 months of daily pain in 2 or more limbs
2. Chronic, widespread pain for at least 3 months
3. Recurrent joint dislocations or frank joint instability, in the absence of trauma (a or b)
   a. Three or more atraumatic dislocations in the same joint or 2 or more atraumatic dislocations in 2 different joints occurring at different times
   b. Medical confirmation of atraumatic joint instability at 2 or more sites

Criterion 3: all 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.
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 (eg, Bethlem myopathy), other hereditary disorders of connective tissue (eg, other types of EDS, Loeys-Dietz syndrome, Marfan syndrome), and skeletal dysplasias (eg, osteogenesis imperfecta). Exclusion of these considerations may be based on history, physical examination, and/or molecular genetic testing, as indicated.

[a] Note that a point may be added to the Beighton score if the 5-point questionnaire is positive (**Box 2**).

Adapted from Malfait F, Francomano C, Byers P, et al. The 2017 international classification of the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet 2017;175(1):8-26; with permission.

Tinkle BT, Levy HP. Symptomatic Joint Hypermobility: The Hypermobile Type of Ehlers-Danlos Syndrome and the Hypermobility Spectrum Disorders. Med Clin North Am. 2019;103(6):1021-1033. doi:10.1016/j.mcna.2019.08.002