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Nutritional Considerations for Hypermobile Ehlers-Danlos Syndrome


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While the hallmarks of hypermobile Ehlers-Danlos syndrome (hEDS) and hypermobility spectrum disorders (HSD) are pain, joint instability, and injuries to soft tissues, most patients with hEDS and HSD have a myriad of manifestations within the gastrointestinal tract that affect dietary tolerance and quality of life. These include irritable bowel syndrome, functional dyspepsia, gastroparesis, constipation, and celiac disease. Other common comorbidities include postural orthostatic tachycardia syndrome and mast cell activation disorders, which may impact fluid and electrolyte balance, food intolerances, and contribute to anxiety around food. Nutritional supplements are commonly used, though research is needed to clarify their potential role in hEDS/HSD management. Patients with hEDS/HSD benefit from the support of a multidisciplinary healthcare team. This review discusses nutritional implications and provides practical recommendations to address the manifestations of hEDS/HSD.

INTRODUCTION

Ehlers-Danlos syndromes (EDS) encompass a group of 14 heritable connective tissue disorders.[1] The most prevalent form of EDS is hypermobile Ehlers-Danlos syndrome (hEDS) and hypermobility spectrum disorders (HSD) with hEDS/HSD appearing to be female-predominant inherited disorders.[2] All types of EDS except hEDS/HSD have identified genetic markers. HSD is also known as joint hypermobility syndrome (JHS), an older term that still appears in research. Key characteristics of hEDS/HSD are pain, fatigue, joint instability, and its consequential injuries to soft tissues.[3] Patients with HSD share most of the features of hEDS, with similar symptoms, disease severity, and treatment strategies.[3] Clinical features are widespread, affecting neurologic, cardiovascular, gastrointestinal, and urogynaecological systems.

The largest prevalence study is from Wales, UK,

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indicating 1:500 (2%) of the general population received a formal diagnosis of hEDS or JHS.[4] Both hEDS/HSD are currently underdiagnosed, with diagnosis typically taking 10+ years.[5] According to an EDS worldwide survey, 97% of people with EDS report that prior to diagnosis, their healthcare team attributed their symptoms to psychological causes.[6] Studies suggest the actual prevalence of hEDS/HSD is closer to 3% of the general population.[4,7]

Management of hEDS/HSD involves relieving symptoms and ensuring sufficient nutrient intake. This review focuses on gastrointestinal (GI) disorders, such as irritable bowel syndrome (IBS), functional dyspepsia (FD), gastroparesis, celiac disease, and other nutrition-related disorders, such as temporomandibular joint (TMJ) dysfunction, eating disorders (EDs), autonomic disorders such as postural orthostatic tachycardia syndrome (POTS) and mast cell activation disorder (MCAD).[8] Practical applications will be emphasized (see Table 1).

Gastrointestinal Manifestations of hEDS/HSD

Gastrointestinal disorders are among the most common manifestations of hEDS/HSD, with studies reporting ~90% of patients experience symptoms of diseases of gut-brain interaction (DGBIs).[8] GI symptoms may include dysphagia, reflux, postprandial fullness, bloating, abdominal pain, nausea, vomiting, diarrhea, and constipation. Patients often attribute symptoms to eating, which can generate food fears and changes in appetite that impact nutritional intake and contribute to disordered eating patterns.[8]

Irritable Bowel Syndrome

Research suggests that up to 62% of people with hEDS/HSD are diagnosed with a subtype of IBS (IBS-diarrhea, IBS-constipation, IBS-mixed, IBS-undefined).[9] Using the ROME IV criteria, IBS is characterized by the presence of recurrent abdominal pain one day a week or more for at least 3 months and the presence of at least two

Table 1. Diet Recommendations for Manifestations of hEDS/HSD

Condition	Diet (as appropriate)
Irritable Bowel Syndrome	• Start with the National Institutes for Health and Care Excellence (NICE) guidelines • If the NICE guidelines are not successful in alleviating symptoms, consider the low FODMAP diet with the elimination, reintroduction, and personalization phases
Functional Dyspepsia	• Consider a trial limiting fatty or spicy foods, wheat, caffeine, and alcohol • Consider a Mediterranean Diet pattern to reduce intake of animal protein and increase intake of fruits and vegetables • Consider a trial of the low FODMAP diet • Have small meals throughout the day • Eat slowly and chew well
Gastroparesis	• Incorporate a small particle size diet with a focus on blending, mashing, or mincing foods • Adjust fiber intake if necessary • Increase movement after meals if possible • Have small meals throughout the day • Consume foods with fat as tolerated. Fat is sometimes tolerated best in liquid form.
Constipation	• Eat two kiwifruit a day • Increase intake of soluble fiber which binds water (e.g., oats, flax) with increased fluid intake • Add foods with natural sorbitol content (e.g., prunes, dried apricots) • For IBS-C, consider a short-term trial of the NICE guidelines or the low FODMAP diet
Celiac Disease	• Adopt a lifelong gluten-free diet • Monitor for nutrient deficiencies
Temporomandibular Disorders	• Switch to pureed foods or soft textures if needed • Cut food into smaller pieces to ease chewing
Postural Orthostatic Tachycardia Syndrome	• Increase fluid consumption to 2-3 liters daily and increase salt up to 6-10 grams unless contraindicated • Consider a lower glycemic diet if appropriate • Monitor symptoms and tailor specific recommendations based on the patient's needs
Mast Cell Activation Disorders	• An experienced RDN should evaluate a diet journal for potential MC triggers • Consider a low histamine diet elimination and reintroduction if indicated

symptoms related to defecation, a change in stool frequency and/or form. Visceral hypersensitivity, central sensitization, autonomic dysfunction, mast cell activation, and/or biopsychosocial factors may also contribute to symptoms of IBS. Symptomatic patients often seek nutrition guidance initially; however, organic disease must be ruled out first if there is unintentional weight loss, anemia, elevated inflammatory markers, or signs of a potential GI bleed.

A first-line approach for IBS management is to implement the NICE (National Institutes for Health and Care Excellence) guidelines, which include:[10,11]

- eating regular, small meals
- eating slowly
- hydrating adequately
- avoiding excessive caffeine, alcohol, or carbonation
- avoiding more than 3 portions of fruit or juice daily
- avoiding polyols for people with loose stools
- reducing fatty foods
- limiting insoluble high fiber foods

Research is limited on the efficacy of the NICE guidelines; however, they are often the initial strategy because of the relative ease of implementation.

If symptoms do not improve, a secondary approach is the low FODMAP diet (LFD) (fermentable oligo, di, monosaccharides, and polyols). The LFD involves a 2–6 week guided elimination diet of osmotically active short-chain carbohydrates, followed by a structured reintroduction phase to learn potential triggers while adding in high FODMAPs, and finally, a personalization phase to maintain intake of FODMAPs that are tolerated well.[10,11] Studies show the LFD reduces GI symptoms, such as bloating, abdominal pain, and diarrhea, in 57-82% of people with IBS.[10] An LFD should only be undertaken with the guidance of a trained Registered Dietitian Nutritionist (RDN).

In a study of 165 patients diagnosed with both IBS and JHS, and controls with IBS only, all subjects followed the LFD.[12] Patients with JHS had greater decreases in abdominal pain and bloating. The patients who had both JHS and IBS-C showed the largest improvement on an LFD compared to IBS-C controls.[12] Further studies are needed to confirm these results and understand the biological mechanism for decreased pain in patients with JHS.

Functional Dyspepsia

The hallmarks of functional dyspepsia (FD) include decreased appetite, postprandial distress, early satiety, nausea, belching, and epigastric pain.[13] Studies found that between 37-86% of patients with hEDS/HSD experience FD symptoms.[13] FD often impairs dietary intake. Limited research supports small, frequent, regular meals, eating slowly, and chewing well. There is potential benefit to limiting fatty or spicy foods, wheat, caffeine or alcohol.[14] Lower adherence to the Mediterranean diet pattern has been associated with worsening of symptoms in FD, thus there may be utility to adopting the Mediterranean diet, which reduces intake of animal protein and increases intake of fruits and vegetables. Also, implementing the LFD has been shown to reduce symptoms.[14]

Gastroparesis

Common gastroparesis symptoms include changes in appetite, nausea, vomiting, early satiety, and unintentional weight loss. A large case-control study compared hospitalized patients with and without EDS and found patients with EDS exhibited a 12.26 higher odds ratio of a concurrent diagnosis of gastroparesis.[15] These results are supported by another study which found 52% of patients with GI symptoms and JHS were diagnosed with gastroparesis.[16] Nutrition interventions to manage gastroparesis include smaller meals, modification of fiber intake, and post-prandial

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movement as tolerated to enhance motility. A small particle size diet, or altering food consistency by blending, processing or mashing food may help expand dietary tolerance (e.g., smoothies, mashed potatoes).[17]

Constipation

Constipation is common; a recent study found 73% of patients with hEDS/HSD had constipation versus 16% of controls.[3] The underlying etiology of constipation in hEDS/HSD is multifactorial and includes DGBIs, delayed motility, small intestinal methane overgrowth, pelvic floor dyssynergia, medication induced constipation, and rectal hyposensitivity.[8,18] Treatment should be individualized, and dietary adjustments may include eating two kiwifruit daily, gradually increasing higher fiber foods, like oats, prunes, or flaxseed, or adding soluble fiber supplements, such as psyllium husk or partially hydrolyzed guar gum.[11,19] Excess fiber intake can potentially aggravate constipation, especially without concurrent adequate water intake. Patients with comorbid rectal hyposensitivity may benefit from biofeedback, which has been studied in hEDS/HSD.[18]

Celiac Disease

One small study found that 16% of people with hEDS/HSD also had celiac disease.[8] A large case control study determined the rate of celiac disease was 5.5 times higher in people with EDS than the average hospitalized patient.[15] Swedish patients with EDS/JHS had an odds ratio of 2.3 of a subsequent celiac diagnosis.[20] A study in children with joint hypermobility (excessively lax joints, without associated pathology) found an odds ratio of 10.9% for positive celiac serology.[21] Further studies are needed; however, celiac testing is prudent for patients with symptoms or a family history.

People diagnosed with celiac disease need to follow a lifelong, strict gluten-free diet and benefit from consultation with an RDN. Newly diagnosed patients tend to be low in vitamins A, D, E, B12, copper, zinc, folate, and iron, and anyone following a gluten-free diet may be deficient in B vitamins, folate, iron, and calcium due to lack of enrichment and fortification of gluten-free products.[22] Nutrient levels should be monitored, with diet modifications and/or supplementation as indicated.

Other Nutrition-Related Manifestations of hEDS/HSD

A range of conditions, including TMJ, POTS, MCAD, and EDs, are frequently found in people with hEDS/HSD. These conditions contribute to the patient's symptom burden and add an additional layer of complexity to eating.

Temporomandibular Joint Disorders

While the literature is limited, 40-100% of people with EDS report headache and jaw pain.[23] A recent case-control study found that TMJ symptoms, including myofascial pain, headache, jaw pain, and disc displacement occurred more in people with hEDS than controls.[23] Dislocations or subluxations may make chewing difficult and compromise nutritional status. Pain with oral care may exacerbate dental problems. Patients with TMJ and hEDS/HSD should be referred to an RDN to ensure adequate oral intake and appropriate food consistencies, and to knowledgeable dentists and physical therapists (PTs) as needed.

Postural Orthostatic Tachycardia Syndrome

POTS is a form of dysautonomia affecting approximately 30% of people with hEDS/HSD.[7] It is characterized by an increase in heart rate of 30 beats per minute (bpm) in adults (40 bpm for adolescents) in the first 10 minutes when moving from a recumbent to a standing position. Patients must have symptoms of orthostatic intolerance, such as palpitations, concentration difficulties, abnormal fatigue, presyncope, or headache for 3 or more months without another explanation.[24]

Nutrition changes are the cornerstones of treatment for POTS, although medication is often needed. POTS involves hypovolemia; treatment expands blood volume via increased fluids, salt, exercise, and decreased fluid pooling with compression garments.[24] Over 90% of people with POTS experience GI symptoms. Most symptoms improve when sitting or recumbent; bloating, constipation and diarrhea generally do not.[7,25] People with concurrent hEDS/HSD and POTS may experience a higher burden of GI symptoms

Table 2. Resources for Hypermobile Ehlers-Danlos Syndrome

Ehlers-Danlos Syndromes

- Ehlers-Danlos Society: **ehlers-danlos.com**
- Ehlers-Danlos Syndrome (EDS) GP Toolkit: **gptoolkit.ehlers-danlos.org**
- Ehlers-Danlos Support UK: **ehlers-danlos.org**
- Hypermobility Syndrome Association (HMSA): **hypermobility.org**
- SEDS Connective: **sedsconnective.org**
- hEDS/HSD Diagnostic Checklist: **ehlers-danlos.com/heds-diagnostic-checklist**
- EDS Diet & Nutrition: **ehlers-danlos.com/international-consortium-working-groups**

Physical Therapy

- Clarkson University Technologia/Leslie Russek PT, DPT, PhD: **webspace.clarkson.edu/~lrussek/research.html**
- Jeannie di Bon, PT: **youtube.com/c/JeannieDiBonHypermobility**

Other

- Dysautonomia International: **dysautonomiainternational.org**
- The Mast Cell Disease Society: **tmsforacure.org**

compared to those with hEDS/HSD without POTS.[25]

Recommendations should be tailored based on physician guidance and co-morbid illnesses, such as cardiac diseases.[26,27] Unless contraindicated, the initial recommendations are 6 grams of salt and 2-3 liters of fluid.[27] Patients can gradually increase salt intake up to 10 grams, with close monitoring of symptoms, and adjustments based on clinical response.[24] Alcohol, caffeine, and dehydration typically worsen symptoms.[26]

Two small studies investigated dietary interventions in people with POTS. In one study, 20 females with POTS (8 also had hEDS) experienced significant improvements in orthostatic and GI symptoms with a 4-week, self-reported gluten-free diet.[28] Another case-control study examined 12 women with POTS who had a history of orthostatic symptoms with high glycemic foods; information on comorbid conditions such as hEDS/HSD was not provided. The study participants experienced a significant increase in tachycardia after consuming 75 grams of glucose, compared to the 13 controls.[29] This preliminary research suggests a gluten-free and/or a low glycemic diet deserve further study. They may be worth exploring for motivated patients who have been screened for celiac disease and are not at risk of an ED.

Mast Cell Activation Disorders

Mast cells (MCs) are white blood cells found in the mucosa and throughout connective tissue and skin. MC diseases include clonal diseases, which are rare and associated with genetic mutations, and non-clonal MCADs, which include mast cell activation syndrome (MCAS).[30] Typically, MCs respond to pathogens; however, in MCADs, MCs may respond to benign stimuli, such as temperature, food, chemicals, medications, physical exertion, stress, etc. and degranulate, causing an inflammatory cascade by releasing histamine, heparin, prostaglandins, and other mediators. MCAD symptoms affect multiple organ systems: gastrointestinal, neurologic, cardiovascular, dermatologic, and respiratory. Symptoms range from mild to anaphylaxis.[30]

The only well-researched treatment for MCADs is avoidance of known MC triggers, especially in the case of anaphylaxis, and MC stabilizing medications, such as cromolyn sodium, ketotifen, or histamine blocking medications.[30]

Controversy exists over diagnostic algorithms for MCADs; however, overall, studies estimate a 24-31% overlap between MCADs and hEDS.[31] MCADs have potential nutritional implications, including risks for bone loss and food restriction. A low histamine diet (LHD) is commonly

recommended, despite a lack of research.[32] Aged and fermented foods are higher in histamine, but there is no universally accepted list of low histamine foods, and no experimental studies examining the clinical impact of an LHD in people with MCAD. One survey of self-reported experiences on an undefined LHD had 51.1% reporting improvement, 19.1% reporting no change and 29.8% of people who were unsure.[33] An experienced RDN should work with patients to identify patterns of foods triggering MC reactions, and advocate for the widest range of foods tolerated.[34]

Eating Disorders

Patients with GI disorders are at increased risk for developing ED and patterns of disordered eating. There is a bi-directional relationship where GI symptoms can lead to food restriction and restriction exacerbates GI symptoms. Avoidant-restrictive food intake disorder (ARFID) is an ED unrelated to weight involving fear of symptoms from eating, such as choking, pain, or nausea.[35] In a 2023 study, 37.9% of people with hEDS/HSD had a positive ARFID screen using the Nine Item Avoidant Scale (NIAS).[36] A positive screen was associated with changing diets, skipping meals, eliminating foods, and seeking or receiving nutritional support, such as enteral feeding.[36]

Patients should be screened to identify an ED, although the NIAS has not been validated for people with GI disorders.[37] An experienced ED specialist can discern the difference between necessary vigilance due to pain, disease management or disordered eating. A multi-disciplinary approach is necessary, including an RDN, psychological support, and medical interventions when appropriate.

Supplement Use in hEDS/HSD

Supplements are widely used; however, research on utility for hEDS/HSD is lacking. Supplements should be discussed with patients reporting use or expressing interest. There are currently no evidence-based recommendations for dietary supplementation to treat hEDS/HSD, nor supplements that will benefit all patients. Supplementation regimens should be based on nutrition assessments of individual patients. Research specific to hEDS/HSD is needed, particularly on the supplements mentioned below.

Antioxidants

Mantle et al. proposed a 12-nutrient and antioxidant protocol intended to address various forms of EDS in 2004.[38] No trials have been published on this. Three studies explored supplement use, and 61-81% of patients with hEDS/HSD report taking supplements.[36,39,40] Patients frequently reported using vitamins C, D and magnesium in all studies and B vitamins and multivitamins in two studies.[39,40]

Collagen

Abnormal synthesis and processing of collagen proteins and the extracellular matrix (ECM) are recognized in EDS, with some of the specific proteins and genetic variants identified.[41] The collagen or ECM variants associated with hEDS/HSD have not yet been identified.[2] Collagen synthesis always requires adequate dietary intake of amino acids and cofactors. However, no data suggests excess collagen from any source or type provides additional benefit for hEDS/HSD.

Folate

A recent review postulates that hEDS/HSD might be due to a common polymorphism known as a methylenetetrahydrofolate reductase (MTHFR) deficiency that prevents the proper usage of vitamin B9, or folate. The solution would be providing the supplemental 5-methyltetrahydrofolate and/or decreasing folic acid supplementation.[42] The authors allude to trials of folate supplementation in patients with hEDS/HSD but did not share the number of patients, the dose used, or if they confirmed that those patients had MTHFR mutations, or the wider context of interactions with the methionine cycle. There are no published trials in patients with hEDS/HSD. Further research is warranted, and more information is needed before practice guidelines can be developed.

CONCLUSION

Patients with hEDS/HSD experience a wide range of manifestations that impact nutrient intake, digestion, and food tolerance and will benefit from specialized nutrition guidance and having access to resources (See Table 2). Common comorbidities, such as DGBIs, other GI disorders, EDs, MCAD, and POTS add additional layers of complexity. Each patient with hEDS/HSD will need a plan tailored to

their individual circumstances. Supplement usage is common, and clinicians should query about usage and evaluate its appropriateness. Clinicians should anticipate that patients will benefit from coordinated support from a multi-disciplinary team including RDNs. ■

References

1. Malfait F, Castori M, Francomano CA, Giunta C, Kosho T, Byers PH. The Ehlers–Danlos syndromes. Nat Rev Dis Primer. 2020;6(1):64.
2. Scicluna K, Formosa MM, Farrugia R, Borg I. Hypermobile Ehlers–Danlos syndrome: A review and a critical appraisal of published genetic research to date. Clin Genet. 2022;101(1):20-31.
3. Aubry-Rozier B, Schwitzguebel A, Valerio F, et al. Are patients with hypermobile Ehlers–Danlos syndrome or hypermobility spectrum disorder so different? Rheumatol Int. 2021;41(10):1785-1794.
4. Demmler JC, Atkinson MD, Reinhold EJ, Choy E, Lyons RA, Brophy ST. Diagnosed prevalence of Ehlers-Danlos syndrome and hypermobility spectrum disorder in Wales, UK: a national electronic cohort study and case-control comparison. BMJ Open.
5. Halverson CME, Cao S, Perkins SM, Francomano CA. Comorbidity, misdiagnoses, and the diagnostic odyssey in patients with hypermobile Ehlers-Danlos syndrome. Genet Med Open. 2023;1(1):100812.
6. Bulbena-Cabré A, Baeza-Velasco C, Rosado-Figuerola S, Bulbena A. Updates on the psychological and psychiatric aspects of the Ehlers–Danlos syndromes and hypermobility spectrum disorders. Am J Med Genet C Semin Med Genet. 2021;187(4):482-490.
7. Tai FWD, Palsson OS, Lam CY, et al. Functional gastrointestinal disorders are increased in joint hypermobility-related disorders with concomitant postural orthostatic tachycardia syndrome. Neurogastroenterol Motil. 2020;32(12):e13975.
8. Thwaites PA, Gibson PR, Burgell RE. Hypermobile Ehlers–Danlos syndrome and disorders of the gastrointestinal tract: What the gastroenterologist needs to know. J Gastroenterol Hepatol. 2022;37(9):1693-1709.
9. Choudhary A, Fikree A, Aziz Q. Overlap between irritable bowel syndrome and hypermobile Ehlers–Danlos syndrome: An unexplored clinical phenotype? Am J Med Genet C Semin Med Genet. 2021;187(4):561-569.
10. Rej A, Avery A, Aziz I, et al. Diet and irritable bowel syndrome: an update from a UK consensus meeting. BMC Med. 2022;20(1):287.
11. Radziszewska M, Smarkusz-Zarzecka J, Ostrowska L. Nutrition, Physical Activity and Supplementation in Irritable Bowel Syndrome. Nutrients. 2023;15(16):3662.
12. Fragkos KC, Keetarut K, Cox A, Eady J, Emmanuel AV, Zarate-Lopez N. Joint Hypermobility Syndrome Affects Response to a Low Fermentable Oligosaccharide, Disaccharide, Monosaccharide and Polyol Diet in Irritable Bowel Syndrome Patients: A Retrospective Study. Gastroenterol Res. 2019;12(1):27-36.
13. Carbone F, Goelen N, Fikree A, Aziz Q, Tack J. Impact of joint hypermobility syndrome on gastric accommodation and nutrient tolerance in functional dyspepsia. Neurogastroenterol Motil. 2021;33(7):e14086.
14. Amerikanou C, Kleftaki SA, Valsamidou E, et al. Food, Dietary Patterns, or Is Eating Behavior to Blame? Analyzing the Nutritional Aspects of Functional Dyspepsia. Nutrients. 2023;15(6):1544.
15. Brooks RS, Grady J, Lowder TW, Blitshteyn S. Prevalence of gastrointestinal, cardiovascular, autonomic and allergic manifestations in hospitalized patients with Ehlers-Danlos syndrome: a case-control study. Rheumatology. 2021;60(9):4272-4280.
16. Loganathan P, Herlihy D, Gajendran M, et al. The spectrum of gastrointestinal functional bowel disorders in joint hypermobility syndrome and in an academic referral center. J Investig Med. Published online November 18, 2023:10815589231210486.
17. Olausson EA, Störsrud S, Grundin H, Isaksson M, Attvall S, Simrén M. A Small Particle Size Diet Reduces Upper Gastrointestinal Symptoms in Patients With Diabetic Gastroparesis: A Randomized Controlled Trial. Am J Gastroenterol. 2014;109(3):375-385.
18. Choudhary A, Vollebregt PF, Aziz Q, Scott SM, Fikree A. Rectal hyposensitivity: a common pathophysiological finding in patients with constipation and associated hypermobile Ehlers–Danlos syndrome. Aliment Pharmacol Ther. 2022;56(5):802-813.
19. Bellini M, Tonarelli S, Barracca F, et al. Chronic Constipation: Is a Nutritional Approach Reasonable? Nutrients. 2021;13(10):3386.
20. Laszkowska M, Roy A, Lebwohl B, Green PHR, Sundelin HEK, Ludvigsson JF. Nationwide population-based cohort study of celiac disease and risk of Ehlers-Danlos syndrome and joint hypermobility syndrome. Dig Liver Dis. 2016;48(9):1030-1034.
21. Sag E, Demir F, Sag S, Guven B, Kalyoncu M, Cakir M. Prevalence of celiac disease in children with joint hypermobility. Acta Reumatol Port. 2021;46(2):134-139.
22. Rubio-Tapia A, Hill ID, Semrad C, et al. American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease. Am J Gastroenterol. 2023;118(1):59-76.
23. Bech K, Fogh FM, Lauridsen EF, Sonnesen L. Temporomandibular disorders, bite force and osseous changes of the temporomandibular joints in patients with hypermobile Ehlers-Danlos syndrome compared to a healthy control group. J Oral Rehabil. 2022;49(9):872-883.
24. Vernino S, Bourne KM, Stiles LE, et al. Postural orthostatic tachycardia syndrome (POTS): State of the science and clinical care from a 2019 National Institutes of Health Expert Consensus Meeting - Part 1. Auton Neurosci. 2021;235:102828.
25. Tu Y, Abell TL, Raj SR, Mar PL. Mechanisms and management of gastrointestinal symptoms in postural orthostatic tachycardia syndrome. Neurogastroenterol Motil.

2020;32(12):e14031.
26. Harris CI. COVID-19 Increases the Prevalence of Postural Orthostatic Tachycardia Syndrome: What Nutrition and Dietetics Practitioners Need to Know. J Acad Nutr Diet. 2022;122(9):1600-1605.
27. Williams EL, Raj SR, Schondorf R, Shen WK, Wieling W, Claydon VE. Salt supplementation in the management of orthostatic intolerance: Vasovagal syncope and postural orthostatic tachycardia syndrome. Auton Neurosci. 2022;237:102906.
28. Zha K, Brook J, McLaughlin A, Blitshteyn S. Gluten-free diet in postural orthostatic tachycardia syndrome (POTS). Chronic Illn. 2023;19(2):409-417.
29. Breier NC, Paranjape SY, Scudder S, et al. Worsening Postural Tachycardia Syndrome Is Associated With Increased Glucose-Dependent Insulinotropic Polypeptide Secretion. Hypertension. 2022;79(5).
30. Hamilton MJ. Nonclonal Mast Cell Activation Syndrome. Immunol Allergy Clin North Am. 2018;38(3):469-481.
31. Theoharides TC, Twahir A, Kempuraj D. Mast cells in the autonomic nervous system and potential role in disorders with dysautonomia and neuroinflammation. Ann Allergy Asthma Immunol. Published online November 2023:S1081120623013972.
32. Daylor V, Gensemer C, Norris RA, Bluestein L. Hope for Hypermobility: Part 2—An Integrative Approach to Treating Symptomatic Joint Hypermobility. Top Pain Manag. 2023;38(9):1-10.
33. Russell N, Jennings S, Jennings B, et al. The Mastocytosis Society Survey on Mast Cell Disorders: Part 2—Patient Clinical Experiences and Beyond. J Allergy Clin Immunol Pract. 2019;7(4):1157-1165.e6.
34. Hamilton MJ, Scarlata Kate. Mast Cell Activation Syndrome–What it is and what it isn't. Pract Gastroenterol. 2020;XLIV(6):26-32.
35. Staller K, Abber SR, Burton Murray H. The intersection between eating disorders and gastrointestinal disorders: a narrative review and practical guide. Lancet Gastroenterol Hepatol. 2023;8(6):565-578.
36. Topan R, Pandya S, Williams S, et al. Comprehensive Assessment of Nutrition and Dietary Influences in Hypermobile Ehlers Danlos Syndrome (CANDI-hEDS) – a cross sectional study. Am J Gastroenterol. Published online November 16, 2023.
37. Fink M, Simons M, Tomasino K, Pandit A, Taft T. When Is Patient Behavior Indicative of Avoidant Restrictive Food Intake Disorder (ARFID) Vs Reasonable Response to Digestive Disease? Clin Gastroenterol Hepatol. 2022;20(6):1241-1250.
38. Mantle D, Wilkins RM, Preedy V. A novel therapeutic strategy for Ehlers–Danlos syndrome based on nutritional supplements. Med Hypotheses. 2005;64(2):279-283.
39. Paiba N, Harris M. Nutritional knowledge, attitudes and dietary behaviours amongst individuals with hypermobility syndromes and associations with co-morbid gastrointestinal symptoms and fatigue: an observational study. Eur J Integr Med. 2023;58:102231.
40. Doyle TA, Halverson CME. Use of complementary and alternative medicine by patients with hypermobile Ehlers–Danlos Syndrome: A qualitative study. Front Med. 2022;9:1056438.
41. Caliogna L, Guerrieri V, Annunziata S, et al. Biomarkers for Ehlers-Danlos Syndromes: There Is a Role? Int J Mol Sci. 2021;22(18):10149.
42. Courseault J, Kingry C, Morrison V, et al. Folate-dependent hypermobility syndrome: A proposed mechanism and diagnosis. Heliyon. 2023;9(4):e15387.

Answers to this month's crossword puzzle: