

hEDS (Hypermobile Ehlers-Danlos Syndrome) Symptoms

Autonomic Nervous System (ANS) Symptoms:

- Abnormal pain processing: Hyperalgesia (increased sensitivity to pain) and allodynia (pain from stimuli that aren't typically painful), often associated with sensory nerve dysfunction and autonomic regulation disturbances. Chronic pain syndromes can be exacerbated by autonomic instability
- Altered pharmacokinetics: Heightened drug sensitivity and altered medication metabolism, leading to unexpected responses to common medications due to autonomic dysfunction, impacting drug absorption, distribution, and clearance
- Autonomic bladder and sexual dysfunction: Beyond neurogenic bladder issues, autonomic dysregulation can contribute to sexual dysfunction, including delayed arousal, vaginal dryness, and difficulty achieving orgasm. These symptoms are caused by the autonomic nervous system's influence on smooth muscle control in the genital area, affecting both urinary and sexual function
- Autonomic fluctuations with physical activity: Individuals may experience significant fluctuations in heart rate, blood pressure, and overall autonomic regulation with physical exertion. This can lead to symptoms such as tachycardia, lightheadedness, dizziness, and fainting with minimal activity, even in the absence of postural changes or exertion
- Bladder dysfunction, electrolyte imbalances, and kidney issues: Neurogenic bladder (NB) or neurogenic lower urinary tract dysfunction leads to symptoms such as urinary urgency, incontinence, frequent nocturia, and difficulty voiding due to autonomic dysregulation of bladder function and poor control over micturition, often caused by nerve problems affecting the brain, spinal cord, or nerves. Additionally, electrolyte imbalances (e.g., low sodium or potassium levels) may result from fluid retention, dehydration, and impaired kidney function. Kidney issues, such as reduced filtration efficiency or chronic kidney disease, may also arise, frequently exacerbated by autonomic dysfunction. Symptoms can include salt cravings, muscle cramping, orthostatic dizziness, and worsening kidney function
- Cognitive and emotional dysregulation: Autonomic dysfunction, particularly dysautonomia, can lead to mood instability, irritability, anxiety, and difficulty managing stress due to the body's altered response to emotional stimuli. This can result in heightened sympathetic activity. Additionally, cognitive dysfunction, including brain fog, poor short-term memory, difficulty concentrating, and challenges with executive function, is common. Individuals may experience post-exertional cognitive fatigue—cognitive fatigue and memory impairment following physical or mental exertion, often accompanied by post-exertional malaise (PEM). This results in delayed onset of cognitive and physical exhaustion after minimal activity, impairing cognitive processing, mental clarity, and information processing
- Dysautonomia (Autonomic Nervous System Dysfunction): A primary characteristic, involving impaired autonomic regulation of heart rate, blood pressure, digestion, thermoregulation, and sweating. This manifests as orthostatic intolerance, postural hypotension, and sympathetic or parasympathetic dysfunction
- Dysphagia and esophageal dysmotility: Dysphagia (difficulty swallowing), globus sensation, and esophageal dysmotility, often due to vocal cord dysfunction (VCD) and autonomic

dysfunction affecting the smooth muscle control of the esophagus. These symptoms can lead to discomfort, regurgitation, and delayed gastric emptying

- Frequent joint subluxations and dislocations: Joint subluxations and dislocations, often occurring with minimal trauma or without clear mechanical strain, can exacerbate pain and trigger autonomic responses such as sweating, dizziness, and heart palpitations. These events are linked to the body's difficulty in stabilizing joints, affecting overall autonomic regulation
- Gastrointestinal dysfunction: Gastroparesis, dysmotility, acid reflux, constipation, diarrhea, and bloating due to autonomic dysregulation of the gastrointestinal tract. This includes impaired stomach emptying and intestinal motility, resulting in chronic digestive discomfort
- Hormonal dysregulation: Fluctuations in hormone levels, especially during periods of menstruation, pregnancy, and adrenal stress, can exacerbate symptoms like joint instability, mood disturbances, fatigue, and vascular instability. Autonomic dysregulation compounds the effects of hormonal changes on the body
- Impaired thermoregulation: This condition leads to heat intolerance, temperature dysregulation, and difficulty maintaining homeostasis, particularly in warmer environments. Symptoms include flushing, cold extremities, excessive sweating (hyperhidrosis), or lack of sweating (anhidrosis), reflecting increased or inadequate sweating. These issues stem from disrupted autonomic control, which affects the body's ability to regulate temperature, contributing to temperature sensitivity, fluctuating body temperature, and altered sweating patterns. Individuals may struggle in warmer environments due to the inability to appropriately regulate heat
- Inflammatory and immune dysregulation: Comorbid conditions such as Mast Cell Activation Syndrome (MCAS) can trigger immune responses that worsen autonomic dysregulation. Symptoms such as flushing, hives, temperature intolerance, and dizziness may occur, overlapping with dysautonomia and complicating symptom management
- Increased sensitivity to medications and environmental factors: Altered pharmacokinetics can lead to heightened sensitivity to environmental factors such as temperature fluctuations, humidity, and even scents, influencing autonomic responses. These sensitivities may result in more pronounced symptoms like dizziness, flushing, or heart palpitations when exposed to triggers
- Possible Interstitial cystitis (IC): Characterized by bladder pain and dysfunction, often related to autonomic dysregulation or neurogenic bladder issues, contributing to urgency, frequency, and discomfort
- Postprandial dyspnea: Dyspnea (shortness of breath) occurring shortly after eating, often related to esophageal dysfunction, vocal cord dysfunction (VCD), or gastroparesis, where gastrointestinal motility issues worsen during digestion and cause difficulty in breathing
- Sensory distortions: Dysesthesia (abnormal sensation), hyperesthesia (increased sensitivity to touch), and altered perception of sensory stimuli (e.g., heightened sensitivity to sound, light, and texture) due to autonomic dysfunction affecting sensory processing and proprioception
- Vasovagal syncope: Individuals with hEDS are prone to vasovagal responses, including fainting triggered by stress, pain, or certain positions. Dysregulation of the autonomic nervous system contributes to the body's inability to properly manage blood pressure during stressors
- Xerostomia and xerophthalmia: Xerostomia (dry mouth) and xerophthalmia (dry eyes), often resulting from autonomic dysfunction, reduced salivary and tear production, and dehydration. These symptoms are common in dysautonomia and contribute to discomfort and difficulty swallowing or speaking

Cardiovascular (CV) System Symptoms:

- Barometric pressure sensitivity: Sensitivity to barometric pressure fluctuations, which may exacerbate headaches, musculoskeletal pain, and joint instability due to changes in blood flow, vascular tone, and sensory processing. Vascular fragility and autonomic dysregulation are central in these responses
- Cardiac dysrhythmias and heart rate variability: Cardiac arrhythmias, including tachycardia, bradycardia, and altered heart rate variability, are commonly observed due to structural and functional abnormalities in the cardiovascular system, such as weakened vascular walls, impaired vascular tone, and abnormal connective tissue properties. These abnormalities can disrupt autonomic regulation of heart rate and blood pressure, leading to symptoms such as palpitations, irregular heartbeats, and exercise intolerance, particularly in response to postural changes or physical exertion
- Cardiovascular structural and functional abnormalities (heart valves and vessels): Pathophysiologic alterations of cardiac valves and vascular structures arising from connective-tissue fragility and extracellular matrix dysregulation characteristic of hEDS. These may include valvular prolapse (most commonly mitral valve), valvular regurgitation of variable severity, aortic root or ascending aortic dilation, and reduced vascular wall integrity leading to abnormal arterial compliance. Such structural and functional impairments can predispose to hemodynamic instability, altered stroke volume, and increased susceptibility to arrhythmias or long-term cardiovascular complications, necessitating careful surveillance and management
- Delayed capillary refill: A slower-than-normal capillary refill time, which refers to the time taken for color to return to the nail bed after pressure is applied, can indicate poor circulatory function due to vascular instability. This delayed response is a sign of compromised blood flow and vascular tone
- Hyperadrenergic state: In some individuals, excessive sympathetic nervous system activation can lead to symptoms like elevated heart rate, high blood pressure, palpitations, and increased anxiety or stress sensitivity, often worsened by physical exertion
- Neurogenic syncope: Neurogenic syncope (fainting) due to impaired circulatory control and vascular instability, often triggered by postural changes, stress, or physical exertion. Orthostatic hypotension and blood pooling are contributing factors
- Orthostatic intolerance and syncope: Orthostatic hypotension, presyncope, and syncope due to poor circulatory control, vascular instability, and impaired autonomic regulation. These episodes often occur with postural changes, such as standing up quickly or after prolonged standing, and are frequently exacerbated by exertion or dehydration
- Tethered or stretched blood vessels: Abnormal stretching or elongation of blood vessels due to compromised connective tissue can result in greater vascular sensitivity, which may lead to vascular tears or increased blood flow fluctuations. These changes can make the vessels more susceptible to damage, causing symptoms such as internal bleeding or localized pain
- Vascular fragility and easy bruising: Weakened blood vessel walls can lead to spontaneous bruising or petechiae (small red or purple spots caused by broken capillaries), a result of vascular instability that affects the integrity of the blood vessels and capillaries

Central and Peripheral Nervous Systems (CNS/PNS) Symptoms:

- Allodynia: Pain elicited by normally non-painful stimuli, often due to nociceptive pathway sensitization or peripheral neuropathy
- Ataxia: Impaired coordination or balance, frequently caused by proprioceptive deficits or CNS (central nervous system) dysfunction, such as cerebellar involvement
- Bladder dysfunction: Neurogenic bladder characterized by symptoms like incontinence, urgency, and frequency, typically due to autonomic or peripheral nerve dysfunction
- Brain fog: Cognitive impairment involving attention, memory, and executive function, often related to central nervous system dysregulation and autonomic dysfunction.
- Chronic headaches: Persistent headache symptoms, commonly arising from musculoskeletal strain, cranial nerve involvement, or autonomic nervous system dysfunction.
- Cognitive dysfunction: Impaired cognitive processes such as memory, concentration, and mental clarity, often associated with central nervous system and autonomic dysfunction.
- Dizziness or presyncope - Lightheadedness or near-syncope resulting from autonomic dysfunction or dysregulated blood flow, often linked to dysautonomia or central nervous system irregularities.
- Dissociation: A psychological state of detachment or altered perception, frequently seen with central nervous system dysregulation or emotional distress.
- Emotional numbness: A reduction or absence of emotional response, often a result of central nervous system strain or autonomic dysregulation.
- Hand tremors: Involuntary shaking or oscillation of the hands, usually linked to peripheral neuropathy or CNS (central nervous system) dysfunction.
- Impaired balance: Difficulty maintaining equilibrium, often caused by proprioceptive dysfunction, cerebellar atrophy, or vestibular issues.
- Impaired temperature sensation: Difficulty in sensing temperature changes

Connective Tissue & Soft Tissue Symptoms:

- Abnormal sitting positions: Hypermobile individuals may adopt positions like sitting double cross-legged, which feel comfortable due to increased joint flexibility but may contribute to joint strain over time
- Adipose tissue abnormalities (structural): Alterations in subcutaneous and visceral fat distribution and integrity arising from connective-tissue fragility and extracellular matrix dysregulation characteristic of hEDS. Defective structural support within adipose depots may contribute to impaired mechanical cushioning, abnormal contouring of subcutaneous tissue, and altered biomechanical interactions with overlying skin and underlying musculoskeletal structures. These changes can influence local tissue resilience, susceptibility to trauma, and overall structural support, potentially exacerbating musculoskeletal strain, joint instability, and impaired soft-tissue protection

- Altered hair texture: Defective collagen and elastin deposition, along with connective tissue dysregulation, affects hair shaft integrity. This results in brittle or frizzy hair and an increased susceptibility to breakage
- Atrophic striae (stretch marks): Stretch marks can develop easily, especially on the hips, abdomen, and thighs, due to the connective tissue's inability to stretch properly. These marks often form during adolescence without significant weight changes, such as gain or loss, as the skin's elasticity is compromised
- Bendable nails: Nails may be long, but tend to bend easily, indicating potential weakness and fragility. When nails are kept long, they may break more easily due to the compromised structural integrity of the keratin, a sign of connective tissue abnormalities
- Cartilaginous structural abnormalities: Alterations in the composition, mechanical properties, and functional integrity of cartilage due to defective collagen synthesis, extracellular matrix dysregulation, and connective-tissue fragility characteristic of hEDS. These abnormalities may affect articular cartilage, costal cartilage, nasal and auricular cartilage, and other fibrocartilaginous structures, resulting in reduced tensile strength, increased susceptibility to deformation, early-onset degenerative changes, joint instability, and compromised load-bearing capacity. Dysfunctional cartilage contributes to chronic musculoskeletal pain, altered joint biomechanics, and progressive degenerative joint disease
- Cellular structural abnormalities (structural): Alterations in the organization, integrity, and function of cells within connective-tissue matrices resulting from defective collagen synthesis, extracellular matrix dysregulation, and inherent connective-tissue fragility characteristic of hEDS. These cellular-level abnormalities compromise tissue architecture, intercellular adhesion, and biomechanical support, contributing to impaired tissue resilience, abnormal force transmission, delayed wound healing, and increased susceptibility to micro-injury across skin, musculoskeletal, vascular, and organ systems
- Changes in skin texture: Associated with connective tissue dysfunction, including thinning skin, easy bruising, delayed wound healing, and an increased vulnerability to external trauma due to impaired collagen and vascular integrity
- Chest cavity: Caused by connective tissue laxity (leading to rib and spine instability), respiratory dysfunction (irregular breathing and chest tightness from autonomic dysregulation), and postural abnormalities (musculoskeletal weakness contributing to rib cage misalignment). These factors can result in a physical indentation in the chest or sensations of discomfort, tightness, or pressure in the chest cavity
- Chronic fatigue: Persistent and overwhelming fatigue, often exacerbated by physical exertion or stress on connective tissues, leading to reduced energy and stamina
- Chronic gastrointestinal issues: Conditions such as gastroparesis, reflux esophagitis, and gastroenteritis may arise due to connective tissue involvement in the digestive system, impacting its structure and function
- Chronic otitis media and recurrent ear infections: Frequently observed in childhood, these conditions are attributed to eustachian tube dysfunction (ETD), altered mucosal immunity, and decreased mucociliary clearance. Immune dysregulation further exacerbates these issues, increasing susceptibility to infections
- Chronic pain: Ongoing, widespread pain, particularly in the joints, muscles, and soft tissues, due to the inability of connective tissues to provide sufficient support and stability. This pain can be exacerbated by physical exertion, changes in weather, or postural imbalances

- Chronic soft tissue injuries: Recurrent issues such as muscle strains, tendon ruptures, and ligament sprains arise from connective tissue weakness, abnormal collagen formation, altered elasticity, and impaired repair mechanisms
- Clumsiness and dropping objects: Clumsiness and frequently dropping things may stem from joint instability, proprioceptive impairments, and muscle weakness. Disruptions in the body's sense of spatial positioning and movement, due to abnormal feedback between muscles, joints, and the central nervous system, contribute to coordination issues and balance deficits. These dysfunctions are compounded by sensory processing impairments and musculoskeletal weakness from ligament and joint laxity, leading to grip weakness, impaired coordination, and an increased tendency to drop objects
- Cognitive difficulties: Symptoms such as brain fog, attention deficits, and memory issues often arise from neurovascular instability or dysautonomia, affecting cerebral blood flow and nervous system function
- Compromised collagen biosynthesis: Defective collagen production leads to reduced tensile strength of connective tissues and delayed or abnormal repair processes. This results in impaired tissue repair, delayed wound healing, and an increased risk of complications in connective tissue structures
- Connective tissue laxity: Characterized by joint hypermobility, skin hyperelasticity, and joint subluxations, this condition leads to musculoskeletal instability, increasing the risk of dislocations and chronic soft tissue injuries, such as ligament sprains, tendon ruptures, and muscle strains. Associated features include snapping hip syndrome, hip subluxations, and ligamentous laxity, which contribute to further joint instability and swelling. Pelvic floor and visceral organ laxity can result in dysfunction such as prolapse and incontinence. Weakened core muscles lead to poor posture, exacerbating musculoskeletal issues, while hypermobility in key joints intensifies these impairments
- Craniofacial connective-tissue features: Distinctive soft-tissue and skeletal characteristics arising from altered connective-tissue integrity in hypermobile Ehlers-Danlos syndrome (hEDS). These may include a narrow or "thin" nasal bridge, reduced upper-lip volume or thin vermilion, and small or hypoplastic earlobes. Such morphologic traits reflect underlying abnormalities in collagen and extracellular matrix organization, contributing to subtle craniofacial dysmorphism and altered soft-tissue elasticity
- Delayed wound healing and abnormal scarring: Hypertrophic or atrophic scarring is linked to defective extracellular matrix remodeling and impaired fibroblast function, resulting in inefficient tissue repair. These issues are often associated with defects in collagen cross-linking
- Dental and oral health issues: Connective tissue abnormalities contribute to gum sensitivity, delayed wound healing, and mucosal fragility. (See 'Oral Symptoms' for more details)
- Dermatographia: Also known as dermographia or dermographism, this condition is characterized by excessive skin marking in response to light pressure. It is likely caused by hyperreactivity of mast cells in the dermis, altered cutaneous vasodilation, or increased vascular permeability
- Dysautonomia: This condition impairs blood flow and nutrient delivery, further weakening connective tissues. In turn, weakened connective tissues compromise blood vessel integrity, exacerbating symptoms such as blood pressure irregularities and heart rate variability. Dysautonomia may also lead to orthostatic intolerance, temperature regulation problems, and other systemic imbalances

- Ears popping and clicking: These sensations result from connective tissue dysfunction affecting the Eustachian tube and temporomandibular joint (TMJ). Hypermobility and laxity in connective tissues, including ligaments and muscles, impair the function of these structures. Weak support tissues in the Eustachian tube disrupt pressure regulation, causing fullness, popping, or clicking sensations. Similarly, TMJ instability due to lax ligaments can lead to misalignment and clicking sounds, which may impact the ear. The root cause is abnormal collagen in connective tissues, leading to joint instability and dysfunction in ear-related structures
- Easily imprinted skin: This condition, indicative of skin fragility or laxity, is marked by thinness, increased susceptibility to bruising, and a tendency for tearing or injury due to collagen deficiency and reduced dermal integrity. Fragility is exacerbated by skin laxity, where excessive stretchability from connective tissue alterations contributes to skin tears, hyperpigmentation, and bruising. Spontaneous bruising or skin tears occur as fragile connective tissue fails to provide adequate structural support to the dermis and vasculature, making the skin prone to trauma from minimal force
- Elbow joint instability due to weakened connective tissue leads to improper alignment and overuse of surrounding muscles and tendons: This results in compensatory strain on muscles like the flexor carpi ulnaris and extensor carpi ulnaris, causing localized pain. Overstretched or damaged soft tissues around the ulna contribute to this pain: the ulnar nerve may become irritated or compressed, leading to pain along its pathway. Increased muscle tension and trigger points due to instability further exacerbate the pain
- Epithelial support abnormalities (structural): Impaired structural support of epithelial tissues resulting from defective extracellular matrix composition, collagen dysregulation, and connective-tissue fragility characteristic of hEDS. These abnormalities compromise the mechanical stability, barrier function, and resilience of epithelial layers across skin, mucosa, and organ linings. Clinically, this may manifest as increased susceptibility to tissue injury, delayed wound healing, mucocutaneous fragility, and impaired resistance to mechanical or environmental stress, reflecting the systemic impact of weakened connective-tissue scaffolding on epithelial integrity
- Excessive skin folding or early-onset wrinkling: Due to skin laxity, early wrinkling and deep skin folds can develop, particularly around the eyelids, neck, elbows, and knees. This may also include ptosis (drooping eyelids) and sagging skin in areas subject to frequent movement or stretching
- Exfoliative dermatitis: Characterized by abnormal skin desquamation (peeling), particularly on the hands and fingers, this condition is linked to collagen instability within the epidermis, compromising skin integrity and repair
- Extracellular matrix abnormalities (structural): Dysregulation of the extracellular matrix resulting from defective collagen, elastin, and proteoglycan composition characteristic of hEDS. Altered ECM structure compromises tissue tensile strength, elasticity, and biomechanical stability, affecting skin, fascia, cartilage, ligaments, tendons, blood vessels, and visceral support structures. These abnormalities contribute to joint hypermobility, musculoskeletal instability, impaired wound healing, vascular fragility, organ ptosis, and functional impairment across multiple organ systems, reflecting the systemic impact of ECM dysregulation on connective-tissue integrity
- Fascial abnormalities (structural): Altered structural integrity and biomechanical properties of fascial tissues due to defective collagen organization, extracellular matrix dysregulation, and connective-tissue fragility characteristic of hEDS. These abnormalities compromise the tensile

strength, elasticity, and load-bearing capacity of fascial planes, predisposing to musculoskeletal instability, impaired force transmission between muscles, joint hypermobility, and chronic myofascial pain. Dysfunctional fascia may also contribute to altered proprioception, postural instability, and increased susceptibility to soft-tissue injury or strain during routine mechanical stress

- Fibroblast dysfunction (structural): Abnormalities in fibroblast activity, including impaired synthesis, organization, and remodeling of extracellular matrix components such as collagen, elastin, and proteoglycans, characteristic of hEDS. Dysregulated fibroblast function compromises tissue tensile strength, elasticity, and structural integrity across skin, fascia, ligaments, tendons, cartilage, and vascular walls. Clinically, this contributes to joint hypermobility, soft-tissue fragility, delayed wound healing, abnormal scar formation, and systemic connective-tissue manifestations affecting musculoskeletal, vascular, and visceral systems

- Fluctuating skin pigmentation and texture: These changes may indicate underlying vascular instability or autonomic dysfunction, which can influence skin tone and overall skin health

- Heightened pain perception (hyperalgesia): Increased sensitivity to pain may occur due to nerve sensitivity or malfunction, often aggravated by the abnormal structure and function of connective tissues

- Hyperhidrosis (excessive sweating): Can occur in response to autonomic dysfunction and is sometimes exacerbated by anxiety or stress

- Increased bruising and impaired wound healing: Due to compromised connective tissue and fragile blood vessel walls, individuals may experience spontaneous, easy, and increased bruising, along with spontaneous hematomas. These issues result from poor circulation, vascular fragility, and impaired tissue support, leading to delayed recovery from injuries and heightened susceptibility to bruising, even with minimal or no trauma

- Joint swelling: Caused by connective tissue instability and inflammation, this condition contributes to joint laxity and increases susceptibility to injury

- Ligamentous laxity: This condition results in joint instability and predisposes individuals to joint subluxations, dislocations, and chronic pain due to reduced ligament strength and an excessive range of motion

- Microtears: Small, often unnoticed tears in connective tissues like ligaments, tendons, and muscles, caused by the fragility of these tissues. These microtears can lead to pain, instability, and an increased risk of injury with minimal trauma or stress

- Muscle wasting and tendon ruptures: Muscle atrophy and an increased risk of tendon ruptures are often compounded by vascular insufficiencies, resulting from compromised connective tissue integrity

- Mucosal fragility: Weakness in connective tissues extends to mucosal membranes, increasing vulnerability to injury or irritation in areas like the gums, nasal passages, and other mucosal linings

- Neurovascular issues and cervical instability: Connective tissue weakness leads to cervical spine instability, causing vertebral misalignment. This can compress or irritate neurovascular structures, including nerves and blood vessels. The resulting tension and movement contribute to skull clicks, often associated with nerve irritation or vascular compression in the cervical region

- Osteopenia or osteoporosis: A decrease in bone density, often observed in people with connective tissue disorders, can lead to increased susceptibility to fractures or bone deformities

- Pelvic floor laxity: Deterioration of connective tissues supporting the pelvic organs can lead to pelvic floor dysfunction, contributing to conditions such as incontinence, prolapse, and discomfort during physical exertion
- Poor posture: Caused by weakness or instability in core muscles and skeletal misalignment, often resulting from inadequate muscular support for hypermobile joints
- Poor scar formation: Wounds may heal poorly, resulting in thin, easily torn scars or abnormal scarring such as hypertrophic (raised) or atrophic (depressed) scars due to impaired collagen synthesis and delayed wound healing
- Prone to keloids: Increased susceptibility to keloid formation due to connective tissue abnormalities, particularly in the body's response to wound healing and scarring
- Possible complex regional pain syndrome (CRPS): A chronic pain condition triggered by injury, involving severe, burning pain, swelling, skin color/temperature changes, and hypersensitivity. Motor symptoms, including dystonia, limited movement, and abnormal postures, may also occur. CRPS is linked to nerve dysfunction and can spread beyond the initial injury site. It is often associated with peripheral neuropathy and may worsen over time
- Recurring ingrown toenails: Repeated occurrence of ingrown toenails, which may be related to hypermobility or irregular nail growth, often influenced by the connective tissue weakness or abnormalities associated with connective tissue disorders
- Smaller bone size: Potentially linked to connective tissue abnormalities, this condition may affect skeletal development and overall bone structure
- Seborrheic dermatitis: Characterized by flaky, oily, and scaly patches, it commonly affects the scalp, face, and upper chest. Symptoms include dandruff and flaky skin, particularly on the scalp. It may be associated with altered sebaceous gland function, often exacerbated by inflammation, and could be linked to immune system dysregulation or mast cell activation
- Skin hyperelasticity: Also referred to as hyper-elastic or hyperextensible skin, this condition is characterized by the skin's ability to stretch beyond normal limits. It is indicative of collagen fiber instability and excessive skin laxity
- Standing with legs crossed, standing on sides of feet, hyper crossing legs: Postural adaptations due to joint instability and hypermobility; a compensatory mechanism to alleviate discomfort or maintain balance in the presence of connective tissue laxity and musculoskeletal weakness associated with connective tissue disorders
- Structural abnormalities: A spectrum of anatomical and biomechanical alterations arising from defective connective tissue matrix integrity (e.g., abnormal collagen/elastin structure or cross-linking), leading to compromised support and stability of joints, skin, ligaments, tendons, and internal organ attachments. In this context, manifestations may include generalized joint hypermobility, recurrent joint instability (subluxations, dislocations), ligamentous laxity, soft tissue fragility, hyperextensible or fragile skin, and altered soft-tissue architecture. Structural deviations may also involve the spine or craniocervical junction, resulting in spinal malalignment (e.g. scoliosis, kyphosis), spinal instability (such as craniocervical instability or atlanto-axial instability), and predisposition to early degenerative changes including premature osteoarthritis, soft-tissue injury, and organ or visceral displacements such as hernias or prolapses. These structural problems contribute over time to chronic musculoskeletal pain, functional impairment, and multi-system complications due to insufficient mechanical support
- Structural body integrity (structural): The preservation of normal body shape, posture, and biomechanical alignment, dependent on connective-tissue strength, elasticity, and extracellular matrix organization. In hEDS, generalized connective-tissue fragility, ligamentous laxity, and

altered collagen structure compromise the ability to maintain skeletal and soft-tissue alignment. Clinically, this may manifest as postural instability, joint hypermobility, organ ptosis, spinal deformities, and altered musculoskeletal mechanics, reflecting systemic failure of connective-tissue scaffolding to preserve normal anatomical form and functional posture

- Structural integrity deficits (structural): Compromised mechanical stability and resilience of tissues due to defective collagen, elastin, and extracellular matrix organization characteristic of hEDS. Impaired structural integrity affects skin, fascia, cartilage, ligaments, tendons, bones, and visceral attachments, leading to hyperextensible joints, joint instability, soft-tissue fragility, organ laxity, and increased susceptibility to injury or deformation under mechanical stress. These deficits contribute to chronic musculoskeletal pain, impaired functional biomechanics, delayed tissue repair, and progressive structural deterioration across multiple organ systems

- Subcutaneous fatty tissue atrophy: Connective tissue abnormalities can lead to the loss of subcutaneous fat, reducing skin padding and making the skin and underlying structures more susceptible to injury

- Tethered spinal cord syndrome: In individuals with hypermobility or other connective tissue abnormalities, this can result in abnormal stretching or tension on the spinal cord, leading to neurological symptoms such as back pain, leg weakness, and bladder or bowel dysfunction

- Thin or translucent skin: The skin, particularly in areas such as the hands, chest, and arms, may appear abnormally thin or translucent due to reduced dermal thickness, increasing the visibility of underlying veins. This can be more pronounced under certain lighting conditions or during colder, drier seasons

- Vascular fragility and skin sensitivity: Increased vascular fragility can lead to easy bruising, delayed wound healing, and blood vessel rupture. Individuals may experience skin discoloration and RD (Raynaud's phenomenon), particularly with cold exposure or changes in blood flow

- Visceral and internal organ laxity (structural): Pathologic malpositioning, displacement, or functional instability of internal organs resulting from generalized connective-tissue fragility, ligamentous insufficiency, and altered extracellular matrix integrity characteristic of hEDS. Reduced structural support of organ attachments compromises biomechanical stability, predisposing to organ ptosis, prolapse, or malalignment across gastrointestinal, genitourinary, and pelvic systems. These abnormalities contribute to gastrointestinal dysmotility (including delayed gastric emptying, constipation, or impaired bowel transit), functional organ instability, increased risk of herniation, and pelvic floor prolapse. Clinically, patients may experience chronic discomfort, pain, urinary or fecal incontinence, and susceptibility to complications arising from compromised visceral support, reflecting systemic connective-tissue weakness and impaired structural integrity of visceral and ligamentous attachments

Endocrine System Symptoms:

- Adrenal dysfunction: Issues such as adrenal insufficiency or overactivity, resulting in symptoms like fatigue, dizziness, poor stress response, and blood pressure fluctuations

- Hormonal imbalances and dysregulation: Disruptions in the regulation of hormones can lead to issues such as impaired blood sugar control, abnormal temperature regulation, and disturbances in growth, contributing to fragile skin, delayed wound healing, abnormal scarring, weight fluctuations, and potential growth delays. These imbalances can also affect metabolic processes and skin integrity

- Hypoglycemia: Difficulty maintaining stable blood sugar levels, leading to symptoms like dizziness, shakiness, fatigue, and fainting
- Thyroid dysfunction: Imbalances in thyroid hormones, leading to symptoms such as fatigue, weight changes, temperature sensitivity, and skin issues

Gastrointestinal (GI) System Symptoms:

- Abdominal discomfort or pain, bloating, gas, cramping, and flatulence: Particularly postprandial, due to gastrointestinal dysmotility, food intolerance, malabsorption, or dysbiosis, due to connective tissue weakness. hEDS patients may experience bloating and gas more frequently due to food intolerances or malabsorption issues, as the connective tissue weakness can impact the functioning of the digestive system
- Abdominal distension and intestinal gas-related pain (connective-tissue): Discomfort or pain arising from excessive intraluminal gas accumulation due to gastrointestinal dysmotility, altered enteric nervous system signaling, and compromised connective-tissue support of the gut characteristic of hEDS. Impaired propulsion, delayed transit, or dysregulated peristalsis can lead to abnormal gas retention, bowel distension, and visceral hypersensitivity. Clinically, this may present as intermittent cramping, bloating, early satiety, abdominal pressure, and discomfort that may exacerbate functional gastrointestinal symptoms such as constipation, diarrhea, or reflux
- Abdominal fullness and early satiety (sensation of excessive satiety after small meals): Often due to delayed gastric emptying or motility dysfunction
- Abnormal motility (e.g., delayed gastric emptying and impaired bowel function): Due to connective tissue weakness affecting the gastrointestinal tract, which can lead to dysmotility and gastrointestinal dysfunction
- Abnormal thirst or excessive nocturnal thirst: Chronic or excessive thirst, particularly nocturnally, despite sufficient fluid intake. This can arise from vascular fragility, where endothelial dysfunction and compromised blood vessel integrity impair fluid distribution and tissue perfusion. Gastrointestinal absorption dysfunction may hinder proper fluid and electrolyte uptake, further exacerbating dehydration and dysregulating fluid homeostasis, resulting in abnormal thirst perceptions
- Acid reflux and esophageal dysmotility: Commonly observed with gastrointestinal dysfunction and impaired esophageal motility, often leading to dysphagia (difficulty swallowing) or impaired esophageal contractions
- Altered bowel movements: Includes constipation, diarrhea, or alternating patterns due to dysmotility
- Bowel dysfunction and incontinence: Caused by pelvic floor dysfunction due to connective tissue disorders and dysfunction (CTD), leading to weakened or hypermobile pelvic muscles and ligaments. This can result in urgency, rushing to the restroom, and accidents. Weakened control over the anal sphincter and compromised pelvic floor support can cause involuntary leakage. Dysautonomia may exacerbate these symptoms by impacting gut motility and bowel regulation
- Changes in bowel habits: Includes constipation and diarrhea
- Chronic constipation alternating with diarrhea: Often due to gastrointestinal dysmotility or motility dysfunction
- Chronic cough: Resulting from aspiration, acid reflux, or associated respiratory complications
- Chronic nausea and early satiety, (fullness after consuming small meals): Often occurring after meals, often without an identifiable cause
- Diarrhea: Frequently linked to food intolerances or motility issues

- Difficulty digesting fatty foods: Often exacerbated by impaired gastric motility
- Digestive issues: Gastrointestinal symptoms of unclear etiology
- Dysphagia (difficulty swallowing): Often due to esophageal dysmotility or muscular weakness
- Esophageal dysmotility: Caused by collagen instability affecting the smooth muscle and connective tissue in the esophagus, this condition impairs coordinated contractions and peristalsis. It can result in symptoms such as dysphagia, regurgitation, and acid reflux, as weakened connective tissue reduces the esophagus's ability to effectively propel food and liquids into the stomach
- Excessive burping or inability to burp: Indicative of gas retention or motility dysfunction
- Food sensitivities to gluten, dairy, high-fat, high-carbohydrate, or high-sugar foods: These can induce gastrointestinal inflammation and discomfort through immune-mediated or non-immune mechanisms. Gluten can enhance intestinal permeability and activate inflammatory pathways, while dairy sensitivity, often resulting from lactase deficiency or immune reactions to milk proteins, can compromise the gut barrier. High carbohydrate and sugar intake may contribute to dysbiosis and increased intestinal permeability, leading to symptoms such as bloating, cramping, and postprandial discomfort
- Functional dyspepsia: A chronic disorder of upper gastrointestinal sensory and motor function characterized by postprandial fullness, early satiety, upper abdominal discomfort, and nausea, often without structural abnormalities. Frequently associated with visceral hypersensitivity, altered gastric accommodation, and impaired gastric emptying
- Gastroesophageal regurgitation (connective-tissue): Retrograde flow of gastric contents into the esophagus resulting from impaired structural and functional integrity of the lower esophageal sphincter and esophageal motility, often associated with connective-tissue fragility in hEDS. Altered collagen composition, reduced tissue tensile strength, and dysregulated neuromuscular coordination contribute to sphincter incompetence and impaired esophageal clearance. Clinically, this may manifest as heartburn, sour or bitter taste, esophageal irritation, nocturnal reflux, or secondary complications such as esophagitis or Barrett's esophagus in chronic cases
- Gastrointestinal dysmotility and functional enteric disturbance (connective-tissue): Abnormal motility and neuromuscular coordination throughout the gastrointestinal tract, resulting from connective-tissue laxity, impaired enteric nervous system signaling, and compromised visceral or neuromuscular integrity characteristic of hEDS. This dysfunction may affect the esophagus, stomach, small and large intestine, and anorectal segments, leading to defective propulsion, sphincter incompetence, impaired peristalsis, delayed gastric emptying (e.g., gastroparesis), and dysregulated bowel evacuation. Clinically, patients may present with gastroesophageal reflux or heartburn, post-prandial fullness, early satiety, nausea, vomiting, abdominal pain, bloating, distension, altered bowel habits (constipation, diarrhea, or mixed patterns), fecal urgency, incontinence, or visceral discomfort. These motility disturbances can impair nutrient absorption, enhance visceral hypersensitivity, and contribute to secondary functional gastrointestinal disorders, reflecting the interplay of structural tissue weakness, autonomic dysregulation, and enteric nervous system dysfunction. In many cases, upper- and lower-GI dysmotility coexist, representing a generalized gut-motor disorder rather than isolated regional impairment
- IBS-mixed (IBS-M): A functional bowel disorder characterized by recurrent abdominal pain associated with alternating constipation and diarrhea, variable stool patterns, and heightened visceral sensitivity. Often exacerbated by dysmotility, psychological stress, food sensitivities, or autonomic dysfunction

- Increased appetite variability: Loss of appetite or excessive hunger, potentially resulting from dysautonomia affecting hunger regulation
- Irritability related to restroom urgency: Behavioral and affective disturbances, including agitation or emotional lability, triggered by the urgent need for urination or defecation. This may result from dysregulation of autonomic and enteric nervous system signaling, impaired bladder and bowel regulation, heightened visceral sensitivity, or altered central processing of gastrointestinal and genitourinary cues. These pathophysiologic disruptions can exacerbate discomfort, stress responses, cognitive strain, and functional impairment during daily activities
- Symptom exacerbation postprandially: Often linked to digestive stress, where the ingestion of food triggers heightened physiological responses, such as increased gastric acid production, altered gut motility, or immune activation, leading to worsened symptoms
- Incomplete bowel movements: Sensation of incomplete evacuation, linked to motility dysfunction
- Intestinal discomfort: Includes cramping, bloating, and abdominal pain postprandially, typically resulting from motility disturbances, GI motility dysfunction, or food intolerances. Primarily due to visceral hypersensitivity or intestinal permeability (potential leaky gut)
- Intestinal permeability (potential leaky gut): Due to weakened connective tissue in the gut lining and increased inflammation, which can contribute to disrupted barrier function and increased gut permeability
- Malnutrition due to impaired nutrient absorption: Often resulting in nutrient deficiencies in vitamins and minerals
- Nutrient or food malabsorption: Including deficiencies in vitamins and minerals, due to gastrointestinal dysmotility, delayed gastric emptying, slowed intestinal transit, visceral hypersensitivity, gut dysbiosis, increased intestinal permeability, connective tissue abnormalities, food sensitivities or intolerances, and reduced bile acid production or pancreatic insufficiency
- Nutrient transport abnormalities (metabolic/connective-tissue): Impaired absorption, distribution, and utilization of macronutrients and micronutrients resulting from gastrointestinal dysmotility, altered enteric nervous system signaling, and connective-tissue fragility characteristic of hEDS. Dysfunctional gut motility, abnormal luminal transit, and compromised structural support of the gastrointestinal tract may reduce efficiency of nutrient uptake, contributing to malabsorption, deficiencies in vitamins and minerals, and impaired metabolic homeostasis. Secondary effects can include fatigue, impaired tissue repair, decreased muscle strength, and exacerbation of systemic manifestations related to connective-tissue and musculoskeletal fragility
- Possible gastroparesis (GP): Characterized by delayed gastric emptying leading to prolonged digestion, bloating, and nausea
- Possible leaky gut syndrome: Increased intestinal permeability, which may contribute to GI symptoms
- Possible ileus: Intestinal obstruction or functional paralysis of the bowel
- Sensation of fullness or tightness in the throat: Often affecting food intake and swallowing
- Vascular fragility: Characterized by defective blood vessel structure and impaired connective tissue support, increasing the risk of spontaneous bruising, easy bleeding, and internal bleeding. This fragility also contributes to poor wound healing, delayed trauma recovery, and elevated hemorrhaging risk, due to abnormalities in the vascular connective tissue matrix. Weakened blood vessel support heightens the risk of gastrointestinal and abdominal bruising

- Visceral hypersensitivity: Increased sensitivity in the gastrointestinal tract, often resulting in exaggerated pain or discomfort in response to normal stimuli due to altered sensory processing
- Water malabsorption: Difficulty absorbing fluids, leading to dehydration
- Weight fluctuations: Unexplained weight loss or gain, frequent unexplained weight changes, often associated with GI dysfunction and malabsorption and GI symptoms, as well as difficulty in absorbing nutrients or altered motility
- Whole-gut dysmotility: Global impairment of gastrointestinal transit affecting the stomach, small intestine, and colon due to connective tissue laxity, smooth muscle dysfunction, and altered neuromuscular signaling. Presents with combined upper and lower GI symptoms, including delayed gastric emptying, constipation, diarrhea, and abdominal pain

Hematological System Symptoms:

- Bleeding tendencies: Individuals with hEDS may exhibit an increased propensity for bleeding, characterized by frequent nosebleeds, excessive bleeding from minor trauma, or prolonged bleeding post-surgery. This is primarily due to the fragility of the blood vessels, which are more susceptible to rupture
- Capillary fragility: hEDS is associated with capillary fragility, where small blood vessels, particularly those near the skin's surface, rupture more easily. This can result in visible bruising or splinter hemorrhages—small petechiae blood spots under the nails—due to the compromised integrity of the vascular walls
- Hematological abnormalities (blood/connective-tissue): Alterations in blood composition, coagulation, and hemostatic function associated with connective-tissue fragility characteristic of hEDS. Defective extracellular matrix and vascular support can predispose to easy bruising, prolonged bleeding, and impaired microvascular integrity. Patients may exhibit subtle platelet or coagulation pathway dysfunction, mucocutaneous hemorrhage, or increased susceptibility to hematoma formation, reflecting the interplay between vascular wall weakness, connective-tissue dysregulation, and hemostatic balance
- Hematopoiesis abnormalities (bone marrow/connective-tissue): Altered production, differentiation, or maturation of blood cells within the bone marrow potentially influenced by connective-tissue fragility and extracellular matrix dysregulation characteristic of hEDS. Defective stromal support or marrow microenvironment integrity can impair hematopoietic niche function, leading to subtle variations in erythrocyte, leukocyte, or platelet production. Clinically, this may manifest as mild cytopenias, impaired hemostasis, increased susceptibility to bruising or bleeding, and alterations in immune response, reflecting the interplay between systemic connective-tissue abnormalities and hematopoietic function
- Iron deficiency and anemia: Chronic bleeding, combined with gastrointestinal issues often present in hEDS, can increase the risk of iron deficiency anemia. This condition impairs the blood's ability to transport oxygen efficiently, thereby contributing to fatigue and exacerbating other systemic symptoms
- Platelet dysfunction and coagulation Defects: Platelet dysfunction in hEDS involves impaired platelet aggregation and coagulation, which leads to a tendency for bleeding despite normal platelet counts. Individuals may experience easy bruising, delayed bleeding cessation from minor cuts, and slower wound healing. This dysfunction is partly due to the inability of platelets to form effective aggregates during the clotting process. Furthermore, the defective collagen in the

vessel walls compromises proper clot formation, thus further increasing the risk of prolonged bleeding

- Prolonged bleeding and easy bruising: The fragility of blood vessels and underlying connective tissue defects in hEDS lead to prolonged bleeding times, delayed clotting, and easy bruising. The vascular fragility disrupts normal clot formation, while platelet dysfunction prevents effective clot development. Together, these factors significantly increase the risk of excessive or prolonged bleeding following even minor injuries

Immune System Symptoms:

- Immunodeficiency: Increased susceptibility to infections and illness due to impaired immune function, often linked to connective tissue abnormalities, which can affect immune cell function and response

- Possible Mast Cell Activation Syndrome (MCAS): Symptoms include anxiety or panic attacks, often triggered by mast cell activation and histamine release, which can affect the central nervous system and contribute to feelings of heightened stress, nervousness, or panic; brain fog, which manifests as difficulties with concentration, short-term memory, mental clarity, and focus, often related to histamine and other inflammatory mediators affecting brain function and neuroinflammation; chest pain, which may be related to mast cell activation affecting the heart or lungs, often linked to histamine or other mediators causing vasodilation or muscle spasms; cramps or muscle pain, occurring due to histamine-induced muscle spasms or gastrointestinal dysfunction, contributing to generalized muscle discomfort; diarrhea, often triggered by dysregulation of the enteric immune system and mast cell degranulation within the gut, leading to increased secretion and motility; fainting (syncope), which is a sudden drop in blood pressure or impaired cerebral perfusion, often secondary to systemic vasodilation or mast cell mediators affecting vascular tone, leading to inadequate blood flow to the brain; fatigue, which is persistent, unexplained exhaustion not proportional to activity levels, often exacerbated by the systemic inflammatory state or autonomic dysregulation associated with MCAS; headaches, commonly triggered by vascular changes, elevated levels of histamine, and other pro-inflammatory mediators released during mast cell activation, which can range from mild to severe, including migraines or tension-type headaches; heat intolerance, due to impaired thermoregulation caused by systemic mast cell activation, leading to an inability to tolerate heat or maintain a normal body temperature, often exacerbated by histamine release; histamine intolerance, where the body experiences abnormal mast cell activation, leading to excessive histamine release, causing symptoms like flushing, itchy skin, headaches, nasal congestion, runny nose, difficulty breathing, heart palpitations, and fatigue; itchiness (pruritus), skin reactions such as rashes and chronic urticaria, typically resulting from histamine release or other mediators involved in mast cell activation, often presenting as dermatographia or dermographism; nausea, which may result from gastrointestinal dysmotility, dysregulation of the enteric nervous system, or direct mast cell degranulation in the gut; nasal congestion, caused by inflammation of the nasal mucosa due to histamine release, leading to swelling and obstructed airflow; presyncope, a sensation of near-fainting, often due to orthostatic hypotension or vasodilation, with mast cell mediators contributing to vascular instability; rapid heartbeat (tachycardia), which results from systemic mast cell activation and autonomic dysregulation, possibly due to histamine's effects on the heart and vasculature or as a compensatory response to hypotension; runny nose (rhinorrhea), caused by increased mucus production and inflammatory

responses in the upper respiratory tract, often triggered by mast cell release of histamine and other cytokines; sleep disturbances, which occur due to histamine's role in wakefulness, making it difficult for many with MCAS to sleep; sudden low blood pressure (hypotension), caused by postural hypotension or acute drops in blood pressure, often induced by mast cell mediators like histamine, prostaglandins, and leukotrienes, leading to dizziness or fainting; swelling (edema), which is peripheral or localized swelling due to fluid retention and leakage from blood vessels, a direct consequence of histamine release; urinary frequency or urgency, which results from bladder irritation, often triggered by mast cell degranulation within the urinary system; dysphagia (difficulty swallowing), choking on spit, air, beverages, food, etc., often clearing throat due to irritation; exercise-induced shortness of breath; chronic cough; hoarseness at the end of a long day; overheating and excessive sweating, especially when around triggers; difficulty swallowing or pain, tightness, itchiness, etc., in the throat

Integumentary System Symptoms:

- Cheilitis and perioral fissuring: Superficial cracking, fissuring, or desiccation of the vermilion border and perioral skin arising from connective-tissue laxity, altered dermal collagen architecture, and reduced skin tensile strength characteristic of hEDS. These structural dermal abnormalities compromise barrier function, predisposing to mechanical injury, chronic irritation, and impaired wound healing. Clinically, this may present as painful fissures, recurrent dryness, or bleeding with minimal trauma, often exacerbated by environmental factors, repetitive mechanical stress, or underlying mucosal fragility
- Connective tissue laxity: Abnormal elongation and looseness of connective tissue fibers result in joint instability, hyperelastic skin, and an increased risk of injury due to compromised structural support of tissues
- Fluid retention: The sensation of fluid accumulation in areas with weakened connective tissue, such as the hands, feet, or abdomen, is due to impaired vascular and interstitial fluid management, leading to localized edema
- Increased risk of hyperpigmentation: Prolonged vascular instability or inflammation can cause localized skin darkening, particularly in areas of trauma or inflammation. This is due to altered blood flow, melanin deposition, and the effects of persistent inflammatory responses
- Increased susceptibility to infections: The fragility of the skin and connective tissue, along with potential immune dysfunction, increases vulnerability to infections. Impaired skin barrier function allows easier microbial entry and may hinder the body's ability to clear infections
- Leg pain: Poor circulation, reduced blood flow to the extremities, and connective tissue abnormalities lead to discomfort or cramping, primarily related to compromised vascular and tissue perfusion
- Localized swelling (edema): Swelling in the extremities, particularly in the legs and feet, arises from the impaired ability of connective tissue to properly regulate fluid balance, leading to fluid retention and visible swelling
- Systemic inflammation: Chronic inflammation can affect the integumentary system, contributing to swelling, discomfort, and changes in skin appearance. The persistent inflammatory response disrupts normal tissue function, exacerbating symptoms like edema and skin tenderness
- Tender or enlarged lymph nodes: Lymph nodes may become enlarged or tender due to inefficient fluid drainage or systemic inflammation. This can occur as a result of the body's

attempt to manage persistent inflammation or infection and may indicate a disruption in normal immune system function

- Thin, fragile skin: Insufficient collagen production and weakened connective tissue support result in skin that is thin, delicate, and prone to tears and bruising. The lack of structural integrity makes the skin highly susceptible to injury

Lymphatic System Symptoms:

- Chronic or recurring lymphedema: Persistent swelling, especially in the lower limbs, due to impaired lymphatic drainage, leading to fluid buildup

- Fatigue: Swelling and fluid retention can cause fatigue as the lymphatic system strains to clear excess fluid

- Fluid retention: A sensation of tightness or fullness in areas where connective tissue is weakened, such as the hands, feet, or abdomen, due to fluid buildup

- Increased susceptibility to infections: Impaired lymphatic circulation can weaken the immune system, making infections more frequent and harder to resolve

- Localized swelling (edema): Swelling, particularly in the legs and feet, caused by inefficient lymphatic drainage in affected areas

- Lymphatic tissue abnormalities (connective-tissue): Structural and functional alterations of lymphatic vessels and lymphoid tissues arising from connective-tissue fragility and extracellular matrix dysregulation characteristic of hEDS. Impaired integrity of lymphatic vessel walls and supporting connective tissue can lead to reduced lymphatic transport, inefficient interstitial fluid clearance, and predisposition to lymphedema or localized fluid accumulation. These disruptions may contribute to impaired immune surveillance, delayed resolution of inflammation, and increased susceptibility to recurrent infections, while also exacerbating tissue edema and secondary musculoskeletal or soft-tissue strain

- Systemic inflammation: Ongoing inflammation affecting the lymphatic system, contributing to swelling, discomfort, and other symptoms

- Tender or enlarged lymph nodes: Lymph nodes may become swollen or painful due to poor drainage or systemic inflammation

Musculoskeletal System (MSK) Symptoms:

- Accessory bony variants or prominent anatomical structures of the elbow: The elbow contains several normal bony prominences (including the olecranon and medial/lateral epicondyles), and some individuals may also have incidental accessory ossicles or mild bony irregularities. In the setting of generalized joint hypermobility, these structures may be more easily palpated or perceived due to reduced soft tissue support and altered joint mechanics. Repetitive mechanical stress and joint instability may also contribute over time to minor enthesopathic or adaptive bony changes at tendon and ligament attachment sites. These findings are often benign and may be asymptomatic, but in some cases can contribute to localized discomfort or altered load distribution across periarticular soft tissues

- Aches and pains: Generalized joint and muscle pain, along with body aches, due to connective tissue involvement

- Arm pain and leg pain: Often associated with joint instability, musculoskeletal dysfunction, and connective tissue involvement, with both potentially resulting from instability in the respective joints and surrounding structures
- Arthralgia (joint pain without inflammation): Characterized by joint pain resulting from instability
- Ataxic gait or limping gait pattern: Characterized by walking in a staggered, uncoordinated manner or with an abnormal weight shift, often due to muscle weakness, joint instability, or neurological issues impacting balance and coordination, including walking with a gait, limping, walking lopsided, or staggered. This can also be caused by the body overcompensating, shifting weight, or preferring one side
- Atlantoaxial instability: Hypermobility in the atlantoaxial joint causing neurological symptoms, including headaches, dizziness, nausea, visual disturbances, or motor weakness due to compression of the brainstem or spinal cord
- Back pain: Due to joint instability, ligament and tendon laxity, soft tissue injuries, skeletal deformities (e.g., scoliosis), nerve compression, muscle weakness, and chronic pain
- Bone pain: Associated with osteopenia or early-onset osteoarthritis
- Carpal tunnel syndrome (CTS) or nerve compression or irritation:
CTS is a condition caused by compression of the median nerve within the carpal tunnel, leading to symptoms such as paresthesia (tingling), hypoesthesia (numbness), and weakness in the thumb, index, and middle fingers. Pain may radiate proximally into the forearm. Symptoms are aggravated by repetitive wrist motions or prolonged compression. Tissue fragility may predispose to nerve compression, while autonomic dysfunction can exacerbate symptoms by affecting vascular tone and circulation, contributing to poor blood flow and worsened CTS
- Chest wall instability: Leading to musculoskeletal discomfort and respiratory issues
- Chronic myofascial pain: Muscle pain that persists due to chronic joint instability and overuse of compensatory muscles, often resulting in tightness, tenderness, and muscle trigger points
- Chronic pain: Often stemming from musculoskeletal or connective tissue dysfunction
- Chronic tendonitis or tendinopathy and tendon tears: Resulting from repetitive stress on joints, leading to inflammation, degeneration, and increased susceptibility to tendon injuries, even with minimal trauma. Tendonitis, characterized by inflammation or irritation of tendons, is often associated with overuse or connective tissue dysfunction
- Decreased joint mobility: Resulting from instability and pain that restrict the range of motion
- Delayed growth or stunted growth: Due to hormonal imbalances and connective tissue abnormalities, particularly in younger individuals
- Difficulty climbing stairs: Due to joint instability, muscle weakness, and proprioception issues
- Early-onset osteoarthritis (OA): Often due to joint hypermobility and excessive joint stress, is characterized by joint pain, stiffness, swelling, instability, and crepitus, typically emerging in adolescence or early adulthood. Contributing factors include ligamentous laxity, muscle weakness, and connective tissue abnormalities
- Episodes of joint locking: Joints temporarily become immobile or stuck in one position and may refuse to pop back into place
- Flat feet (pes planus): Resulting from lax connective tissues and ligaments that fail to support the foot arches, leading to excessive pronation. This misalignment causes discomfort, strain, and instability in the feet, ankles, knees, and hips

- Foot and ankle instability: In addition to flat feet, individuals may experience compromised ligamentous support, increasing the risk of sprains, falls, and difficulty with prolonged walking or standing
- Growing pains in childhood: Likely caused by musculoskeletal developmental stress, resulting in discomfort in the limbs, particularly during periods of rapid growth
- Hand weakness: Reduced muscle strength or control in the upper limbs, often due to neuropathy, motor dysfunction, or musculoskeletal instability
- Headaches: Particularly occipital headaches, often related to cervical instability or musculoskeletal dysfunction
- Hyperextension of joints: Joints moving excessively beyond the normal range of motion due to connective tissue laxity
- Increased joint laxity: Resulting in joint instability and a higher likelihood of subluxations or dislocations
- Increased joint pain: Often worsened by weather changes or physical activity, particularly in hypermobile joints, and linked to a higher risk of ligament tears or fractures due to ligamentous laxity and weakened connective tissue
- Increased risk of recurrent sprains and strains: Including ligamentous injuries such as sprains and tears, due to joint instability, ligamentous laxity, and muscle weakness
- Instability in weight-bearing joints: Difficulty stabilizing weight-bearing joints, such as the knees, hips, and ankles, due to ligamentous laxity and muscle weakness
- Intervertebral disc abnormalities (connective-tissue): Structural and functional alterations of the intervertebral discs resulting from connective-tissue fragility, extracellular matrix dysregulation, and impaired collagen integrity characteristic of hEDS. These abnormalities may include decreased disc hydration, reduced tensile strength of the annulus fibrosus, and altered biomechanical resilience of the nucleus pulposus, predisposing to early degenerative changes, disc bulging or herniation, and compromised spinal load distribution. Clinically, this can manifest as chronic axial spinal pain, reduced spinal stability, increased susceptibility to injury, and secondary musculoskeletal strain due to impaired shock absorption and altered segmental motion
- Intervertebral disc irritation and dysfunction (connective-tissue): Inflammatory or mechanical stress-related compromise of intervertebral disc integrity resulting from connective-tissue fragility, annulus fibrosus weakness, and altered extracellular matrix characteristic of hEDS. These changes can lead to disc bulging, localized annular tears, or altered nucleus pulposus biomechanics, causing axial spinal pain, segmental instability, or radicular symptoms secondary to nerve root irritation. Clinically, patients may present with chronic back pain, exacerbation with mechanical loading, reduced spinal flexibility, and increased susceptibility to degenerative disc disease or recurrent disc injury
- In-toeing: A gait abnormality with inward rotation of the toes or knees, often due to femoral anteversion or tibial torsion, commonly observed in childhood and causing altered biomechanics and potential discomfort
- Joint or systemic hypermobility: Characterized by frequent subluxations, dislocations, or instability resulting from ligamentous weakness and connective tissue laxity
- Joint instability: Leading to pain and increased risk of subluxation or dislocation, particularly during physical activity, due to insufficient support from ligaments and tendons
- Joint crepitus: Characterized by cracking, popping, clicking, or grinding sounds, commonly linked to hypermobility or joint dysfunction

- Joint stiffness: Occurs following periods of inactivity, often resulting from synovial fluid depletion or joint instability
- Joint swelling: Often results from inflammation or trauma, leading to fluid accumulation in the joint
- Knees and hips giving out: Caused by joint instability or hypermobility, where weakened ligaments and connective tissues fail to provide adequate support, leading to sudden loss of control or function in the knees and hips
- Motor dysfunction: Characterized by gait instability, poor coordination, and tremors, often due to musculoskeletal impairments, joint instability, and connective tissue weakness. This leads to difficulty maintaining balance, frequent subluxations, and challenges with fine motor tasks. Muscle weakness and soft tissue injuries are common, further contributing to instability and impairing movement. The inability of connective tissues to provide proper support intensifies mobility challenges, often resulting in pain and difficulty with tasks requiring strength or stability
- Muscle and connective tissue dysfunction: Leads to weakness, fatigue, and pain due to impaired tissue support and function
- Muscle atrophy, weakness, and reduced endurance: Often result from joint instability and insufficient muscle support, impairing overall function
- Muscle fatigue: Often caused by overexertion or weakness due to joint instability, leading to reduced endurance and function
- Muscle tension: Often resulting from instability or overuse, leading to tightness, discomfort, and potential muscle strain
- Muscle tightness: Often caused by spasms related to connective tissue laxity or muscle overuse, leading to discomfort and restricted movement
- Muscle weakness and hypotonia: Resulting from reduced muscle tone, leading to joint instability and impaired musculoskeletal support. This causes difficulty with posture and movement, exacerbating instability due to insufficient muscle strength
- Muscular imbalances: Weakness in certain muscle groups, especially stabilizing muscles, can lead to imbalances, contributing to postural problems, pain, and increased injury risk
- Musculoskeletal deformities: Including flat feet and other structural changes, potentially resulting from chronic instability or overuse
- Musculoskeletal movement abnormalities: Impaired joint and limb function resulting from generalized connective-tissue laxity, ligamentous insufficiency, and altered musculoskeletal biomechanics characteristic of hEDS. These abnormalities manifest as joint hypermobility, recurrent subluxations or dislocations, reduced proprioceptive acuity, and compromised postural stability. Functional consequences include altered gait patterns, impaired balance, increased susceptibility to soft-tissue injury, muscle fatigue, and chronic musculoskeletal pain. Over time, these biomechanical instabilities may contribute to early-onset degenerative joint disease, altered load distribution, and progressive functional limitation
- Musculoskeletal pain: Can lead to deformities, dislocations, or secondary conditions such as osteoarthritis or tendonitis
- Myalgia: Includes muscle pain, soreness, cramping, and spasms, often linked to overexertion or connective tissue dysfunction. It may also involve cramps due to electrolyte imbalances or instability in muscle function, and spasms or muscle twitches associated with neurological dysfunction or connective tissue instability

- Neck pain and stiffness: Related to cervical spine instability, muscle dysfunction, or joint hypermobility causing strain or subluxation in the cervical vertebrae, especially in certain head positions, as well as back and spinal pain from connective tissue laxity, poor joint stability, and muscle weakness
- Occipital or tension headaches: Often caused by cervical instability or musculoskeletal dysfunction, leading to referred pain or tension in the head and neck region
- Osteopenia: Characterized by reduced bone density, leading to increased bone fragility and a higher risk of fractures
- Overstretching injuries: Resulting from hypermobility and fragile connective tissue, leading to sprains, strains, and soft tissue injuries with minimal trauma or overstretching
- Overuse injuries: Caused by excessive stretching or instability in musculoskeletal structures, leading to strains, sprains, and other soft tissue damage
- Pain due to altered biomechanics: Musculoskeletal pain may be exacerbated by altered movement patterns, such as compensation for joint instability, which can lead to secondary issues like muscle overuse or misalignment
- Pelvic floor dysfunction: A condition where the pelvic floor muscles do not function properly, leading to symptoms like urinary incontinence, pelvic pain, and difficulty with bowel movements
- Pelvic instability: In addition to pelvic pain, the instability in the pelvic joints (e.g., sacroiliac joint dysfunction) can lead to issues such as urinary or bowel dysfunction, as well as difficulties with activities requiring core strength or stability
- Pelvic pain: Chronic discomfort in the lower abdomen or pelvis, often associated with underlying musculoskeletal or organ-related causes
- Possible ankylosing spondylitis (AS), chronic inflammatory arthritis that may be associated with musculoskeletal and spinal dysfunction
- Possible bone density issues: Resulting from abnormal connective tissue function, weakened collagen synthesis, and impaired bone matrix integrity, these issues affect the skeletal system's structure and resilience. They can lead to decreased bone strength, increasing the risk of fractures, osteopenia (low-bone mineralization), and osteoporosis (low-bone density)
- Possible bulging discs: A condition where the discs in the spine protrude beyond their normal boundary. Symptoms include localized pain, numbness or tingling in the extremities, muscle weakness, and pain that radiates down the arms or legs depending on the location of the bulging disc
- Possible cervical spondylosis: A condition involving the wear and tear of the cervical spine (neck) due to aging. Symptoms include neck pain and stiffness, headaches, numbness or tingling in the arms and hands, and weakness in the limbs
- Possible congenital myopathy (CM): Characterized by hypotonia (low muscle tone), delayed motor milestones, coordination difficulties, and facial muscle weakness
- Possible degenerative disc disease (DDD): A condition in which the intervertebral discs lose hydration and elasticity, leading to pain, stiffness, and in some cases, nerve compression
- Possible fibromyalgia (FN): A chronic pain syndrome frequently associated with central sensitization, characterized by widespread pain and tenderness that may overlap with musculoskeletal pain but is more diffuse and involves soft tissue. It also contributes to chronic fatigue and sleep disturbances
- Possible femoroacetabular impingement (FAI) syndrome: A condition where abnormal contact occurs between the ball (femoral head) and socket (acetabulum) of the hip joint, leading to hip pain and restricted movement. This can manifest as cam impingement (where the femoral head is

misshapen, creating a bump that causes friction against the acetabulum), pincer impingement (where the acetabulum overcovers the femoral head), or mixed impingement (a combination of both), potentially resulting in damage to the cartilage or labrum over time

- Possible hip dysplasia (HD): Hip dysplasia refers to a condition where the hip socket (acetabulum) is too shallow to properly support the femoral head (the ball of the hip joint), leading to dislocations or subluxations. It is primarily a developmental or structural abnormality affecting the joint's anatomy, often present from birth and usually involving the bones and cartilage. HD is characterized by joint instability, abnormal articulation, and an increased risk of subluxation, with symptoms like clicking, popping, grinding, hip pain, potential hip subluxations, limited hip mobility, restricted movement or range of motion, stiffness, uneven gait, difficulty standing or walking for extended periods, and increased wear and tear on the hip, all of which are linked to connective tissue laxity and muscular imbalances

- Possible hypermobility spectrum disorder (HSD): A condition characterized by joint hypermobility and associated symptoms such as pain, instability, and musculoskeletal dysfunction

- Possible joint hypermobility syndrome (JHS): Characterized by joint hypermobility, recurrent joint subluxations or dislocations, musculoskeletal pain, instability, soft tissue injuries, easy bruising, fatigue, proprioceptive deficits, and gastrointestinal disturbances (e.g., bloating, constipation). Symptoms are associated with connective tissue abnormalities and impaired musculoskeletal function

- Possible occipital neuralgia (ON): A condition characterized by pain due to nerve compression or irritation at the base of the skull

- Possible tethered spinal cord syndrome (TSCS): In some cases, spinal cord tethering can occur due to connective tissue laxity or abnormal spinal alignment, leading to motor deficits, sensory disturbances, and chronic pain

- Posterior pelvic tilt: This can occur when there are imbalances such as tight hamstrings or weak hip flexors and lower back muscles. In some cases, people might adopt this posture as a way to compensate for hypermobility or to stabilize a pelvis that is prone to instability

- Postural difficulties: Including poor posture or inability to maintain a stable posture due to joint instability and muscle weakness

- Postural Orthostatic Tachycardia Syndrome (POTS)-related musculoskeletal symptoms: Musculoskeletal symptoms such as muscle fatigue, cramping, and weakness can be exacerbated by orthostatic stress and poor circulation, potentially contributing to overall joint instability

- Restricted movement after injury: Due to instability, swelling, or musculoskeletal dysfunction

- Rubber band sensation in joints: Often associated with hypermobility or ligamentous laxity

- Sacroiliac joint dysfunction and potential spinal misalignments: Often resulting from instability in the pelvic region

- Sensation of fullness in the throat: Often caused by esophageal motility dysfunction or cervical instability

- Short stature: Commonly observed in certain forms of Ehlers-Danlos Syndrome or connective tissue disorders, often due to abnormal growth patterns or skeletal involvement

Shoulder instability: A condition characterized by recurrent dislocations or subluxations of the shoulder, often triggered by overhead activities. It can result in pain, weakness, and a limited range of motion

- Skeletal abnormalities (musculoskeletal/connective-tissue): Structural and functional deviations of the musculoskeletal system resulting from connective-tissue laxity and altered extracellular

matrix integrity inherent to HSD/hEDS. These may manifest as generalized joint hypermobility, recurrent joint instability (subluxations or dislocations), abnormal joint alignment, and altered bone or soft-tissue architecture — for example flat feet, shallow joint sockets, spinal curvatures (scoliosis, kyphosis, lordosis), or marfanoid body habitus. Chronic joint instability and repeated micro- or macro-trauma contribute over time to degenerative changes including early-onset osteoarthritis, decreased bone mineral density or reduced cortical bone mass, muscle hypotonia with relative underdevelopment of musculature, impaired proprioception and motor coordination, and persistent musculoskeletal pain

- Sneezing, laughing, choking, coughing, or yawning: Can cause dizziness, near-fainting, musculoskeletal pain, or muscle strain due to instability, muscle fatigue, changes in blood pressure, or excessive stress on connective tissues
- Soreness after rest: Due to joint instability and muscle fatigue
- Spinal instability: Can lead to pain and misalignments, with an increased risk due to connective tissue laxity, hypermobility, and poor joint stability
- Tendon and ligament laxity: Contributes to joint instability, frequent subluxations, and a rubber band sensation due to weakened connective tissues
- Tendon weakness or pain: Resulting from connective tissue laxity, increasing the risk of tendon tears or injuries due to reduced structural support
- Temporomandibular joint (TMJ) dysfunction: Characterized by jaw muscle fatigue from overuse or dysfunction of the temporomandibular joint, causing discomfort and jaw pain due to joint instability or misalignment. Symptoms may include limited jaw mobility, increased risk of subluxations or dislocations from connective tissue weakness, and a heightened risk of lockjaw, characterized by muscle spasms or immobility due to TMJ dysfunction or musculoskeletal instability
- Trouble opening things: Difficulty with tasks like opening jars or bottles is often due to joint instability, muscle weakness, and hypermobility, which impair grip strength and coordination. Connective tissue abnormalities and proprioception issues can further reduce hand stability and neuromuscular control
- Weak grip strength: Due to connective tissue instability affecting muscle function and joint stability. Wrist pain, often associated with joint instability or ligamentous laxity
- Weakness or numbness in limbs: Commonly associated with motor neuropathy, peripheral nerve involvement, or central neurological dysfunction affecting muscle strength and sensation
- Wrist instability and injuries: Excessive joint laxity and instability in the wrists can contribute to pain, weakness, and an elevated risk of subluxations. These issues are often exacerbated by repetitive hand movements or weight-bearing activities

Neurological System Symptoms:

- Ataxia: The impaired ability to coordinate voluntary movements, affecting balance, gait, and posture. It results from joint instability, proprioceptive dysfunction, and muscle weakness, which disrupt coordination. Chronic pain and fatigue further compound this neurological impairment
- Atlantoaxial instability: Hypermobility in the atlantoaxial joint (between the first and second cervical vertebrae) can cause neurological symptoms, such as headaches, dizziness, nausea, visual disturbances, or motor weakness, due to compression of the brainstem or spinal cord
- Blurred vision: Visual disturbances, often linked to autonomic dysfunction, particularly related to fluctuations in blood pressure and vascular tone, or neurological impairments affecting ocular control

- Brain fog: Cognitive deficits including impaired concentration, memory problems, and mental clouding, commonly associated with neuroinflammation, central sensitization, and dysregulated ANS (autonomic nervous system) functioning
- Burning skin sensation: Often related to small fiber neuropathy or sensory disturbances caused by autonomic dysfunction, where nerve damage or dysregulation leads to abnormal skin sensations, including a burning or tingling feeling
- Central sensitization and neuroinflammation: Pathological processes where the central nervous system becomes hyper-responsive to stimuli, contributing to heightened pain perception (allodynia) and generalized neurological dysfunction, often exacerbated by autonomic dysfunction
- Low CSF headaches: Can cause neurological symptoms such as dizziness, fatigue, cognitive disturbances, postural headaches, visual disturbances, pressure, fullness, or “sloshing” in the brain, clear fluid drainage from ears or nose, nerve "brain zaps," tinnitus, hearing loss, neck stiffness or pain, photophobia (sensitivity to light), cognitive brain fog, mood changes, lightheadedness or near fainting, photopsia (visual disturbances), dural instability, with increased risk due to connective tissue abnormalities
- Chronic headaches: Frequently associated with vascular dysregulation, autonomic dysfunction, and musculoskeletal tension, often manifesting as tension-type, or cluster headaches
- Chronic pain syndromes (e.g., fibromyalgia): Widespread musculoskeletal pain and tenderness that overlap with neuromuscular dysfunction, often exacerbated by muscle weakness, instability, and sensory disturbances. This pain can significantly impact muscle function and coordination
- Clumsiness: Often due to neurological dysfunction, affecting coordination and motor control
- Cognitive dysfunction: Marked by difficulties with concentration, short-term memory, and mental clarity, commonly arising from neuroinflammation, autonomic dysregulation, and cognitive overload. This can include memory issues after exertion, where cognitive function becomes impaired following physical or mental activity. Mental fatigue is also a frequent symptom, characterized by a feeling of cognitive exhaustion or difficulty processing information, often exacerbated by stress or prolonged activity
- Cognitive overload: A state of mental fatigue that arises after minimal exertion or exposure to environmental stimuli, often resulting in impaired cognitive function, memory lapses, and a sense of mental exhaustion. This condition is frequently triggered by autonomic dysregulation, neuroinflammation, or chronic pain, leading to reduced cognitive performance and difficulty processing information efficiently
- Cognitive processing delays: Delays in cognitive function, including executive dysfunction, such as difficulty with planning, organizing, and decision-making. These delays are often attributed to neuroinflammation, chronic pain, or autonomic dysfunction, all of which can impair the CNS' (central nervous system) capacity to process information in a timely manner
- Crawling, squeezing feelings: These sensations, often described as a crawling or squeezing feeling on the skin, can be associated with neuropathy or sensory disturbances resulting from connective tissue issues, where nerve function is affected by underlying connective tissue abnormalities
- Delayed response to stress: Impaired ability to regulate physiological and emotional responses to stress, often due to ANS (autonomic nervous system) dysregulation and an inadequate response to physical or psychological stimuli
- Difficulty balancing: Often caused by proprioceptive dysfunction or impaired sensory processing, this condition affects the body's ability to maintain stability and coordination

- Difficulty with fine motor skills: Impaired control and coordination of small muscle movements, frequently caused by neurological dysfunction, muscle weakness, and joint instability, including difficulty holding objects and dropping everything
- Dissociation: A neurological phenomenon involving detachment from reality, often occurring as a response to overwhelming sensory input or autonomic dysregulation, leading to emotional numbness or a feeling of detachment from one's body or surroundings
- Dizziness and feeling faint with positional changes (e.g., lying down, sitting, or standing): These symptoms can indicate autonomic dysfunction, such as orthostatic hypotension or vestibular dysfunction, leading to inadequate blood flow to the brain or disrupted balance regulation. This can result in dizziness, lightheadedness, or a sense of near-fainting (presyncope) when changing positions, including lying down, sitting, or standing. In severe cases, this may progress to syncope (fainting), often accompanied by a feeling of imbalance or vertigo
- Ear pain or discomfort: Often a result of neuropathic pain, cranial nerve involvement, or referred pain from cervical spine instability affecting the auditory and vestibular systems
- Emotional numbness: Difficulty processing or connecting with emotions, frequently associated with autonomic dysregulation, neuroinflammation, or cognitive impairment, leading to a diminished emotional response
- Episodes of fainting (syncope): Caused by autonomic dysfunction, often related to orthostatic hypotension, vascular instability, or impaired autonomic regulation of blood flow
- Excessive daytime fatigue: Resulting from disrupted sleep quality due to autonomic dysregulation, neurological impairment, or dysregulation of the body's natural sleep-wake mechanisms. This can lead to increased sleepiness during the day. Sleep disturbances such as restless legs syndrome or parasomnias may arise from CNS (central nervous system) dysfunction, further impairing sleep quality and exacerbating fatigue
- Frequent or excessive yawning or sleepiness: Often related to autonomic dysregulation affecting sleep-wake cycles, causing excessive daytime fatigue or disrupted sleep patterns
- Hand tremors, due to autonomic dysfunction, joint instability, neuropathy, muscle weakness, and CNS (central nervous system) dysfunction
- Hand weakness: Reduced muscle strength or control in the upper limbs, often due to neuropathy, motor dysfunction, or musculoskeletal instability affecting hand function
- Headache: Tension headaches caused by muscle strain or weakness in the neck and shoulders due to cervical instability or hypermobility, often triggered by poor posture, compensatory muscle strain, or fatigue from other connective tissue disorder symptoms. These headaches present as dull, tight pressure, often described as a band around the head, especially around the temples, neck, or shoulders, and are aggravated by poor posture, muscle fatigue, or stress. Cervicogenic headaches, originating from cervical instability or misalignment of the neck, cause sharp or throbbing pain, often unilateral, and can be triggered by neck movements or positions. Associated symptoms include neck pain, stiffness, and dizziness. Sinus headaches, not directly linked to connective tissue disorders but possibly coexisting with sinus congestion, inflammation, or infection, cause pressure and pain around the eyes, cheeks, and forehead, with associated symptoms of nasal congestion, facial tenderness, and fever. CSF leak headaches (spinal headaches) caused by spontaneous cerebrospinal fluid (CSF) leaks, more common in individuals with connective tissue disorders, lead to low-pressure headaches worsened by standing and improved by lying down. These headaches often feel dull and pressure-like, sometimes in the temples or base of the skull, with associated symptoms including nausea, dizziness, neck stiffness, photophobia, tinnitus, cognitive fog, and visual disturbances. Spinal

headaches, linked to CSF leaks common in hEDS, involve positional headaches worsened by sitting or standing and alleviated by lying down, with pressure felt in the temples, forehead, or base of the skull. Associated symptoms include nausea, dizziness, neck stiffness, tinnitus, cognitive fog, and photophobia, all linked to cervical instability, muscle strain, CSF leaks, and neck-related issues

- Head and neck pain due to cranial nerve dysfunction: Cranial nerve involvement as a result of vascular compression or joint instability, there can be cranial nerve involvement leading to symptoms such as visual disturbances, tinnitus, or difficulty swallowing
- Hearing distortion: Caused by dysfunction in the auditory processing pathways or issues within the inner ear, such as fluid imbalance or vestibulocochlear nerve dysfunction. This may lead to distorted sound perception, including ear fullness, muffled or "echoing" sounds, or sensitivity to specific frequencies. It can also be associated with autonomic dysregulation or temporomandibular joint (TMJ) dysfunction
- Heightened pain sensitivity (allodynia): Painful responses to non-noxious stimuli, often a result of central sensitization, neuropathic involvement, or peripheral nerve dysfunction
- Heightened pressure sensitivity: Abnormal response to pressure or touch, often exacerbated by changes in barometric pressure, leading to heightened pain perception. This is linked to hyperalgesia, neuropathy, and soft tissue hypermobility, contributing to exaggerated pain sensitivity and discomfort, and is further influenced by autonomic dysregulation
- Impaired fine motor control and hand weakness: Often due to neuropathic conditions, including peripheral neuropathy or central nervous system dysfunction, affecting dexterity and coordination
- Impaired or dysregulated proprioception: Difficulty sensing the position and movement of joints, often resulting from neurological dysfunction, nerve damage, or sensory processing issues. This leads to challenges with spatial awareness, body position sense, instability, and increased risk of falls, particularly in the absence of visible cues, and can contribute to coordination difficulties
- Impaired temperature sensation: Abnormal temperature perception, often due to peripheral or central neuropathy, leading to increased sensitivity to heat or cold, or an inability to correctly sense temperature changes
- Increased fatigue after mental exertion: Caused by cognitive overload resulting from hypermobility-related instability and autonomic dysfunction, this condition leads to reduced mental endurance and heightened exhaustion following cognitive activities
- Increased risk of transient ischemic attacks (TIAs): Cervical instability or vascular dysregulation can predispose individuals to brief interruptions in blood flow to the brain, leading to TIA-like symptoms such as temporary vision loss, numbness, or difficulty speaking
- Increased sensitivity to sound (hyperacusis): A heightened sensitivity to auditory stimuli, often due to central nervous system dysfunction, which can amplify normal sounds, leading to discomfort or pain
- Intracranial hypotension (low CSF pressure): Associated connective tissue fragility causing spontaneous CSF leaks, categorized as neurological (CSF-related), vascular (affecting circulation and brain perfusion)
- Motor and sensory dysfunction: Includes altered sensory perception, movement coordination difficulties, muscle weakness, and impaired sensory processing. These issues often result from peripheral neuropathy, central nervous system involvement, and musculoskeletal instability

- Neck pain and stiffness: Frequently related to cervical spine instability, muscle dysfunction, or joint hypermobility causing strain or subluxation in the cervical vertebrae
- Neurogenic bladder symptoms: Bladder dysfunction due to autonomic nervous system involvement, leading to difficulty with urinary retention, urgency, frequency, or incontinence
- Neurogenic muscle cramps: Cramps or spasms in muscles that are triggered by nerve dysfunction rather than just overuse or dehydration
- Neuropathy and neuropathic pain: Peripheral neuropathy, often manifesting as small fiber neuropathy (SFN), results in burning, shooting, and stabbing pain, tingling (“pins and needles”), sensitivity to touch (allodynia), numbness or weakness, typically linked to nerve damage, compression, or dysfunction in the peripheral nervous system. Neuropathic pain can arise from central sensitization, leading to increased pain sensitivity to normal stimuli. Dysautonomia exacerbates these symptoms by disrupting autonomic regulation, contributing to erratic blood pressure (including orthostatic hypotension), temperature sensitivity, and sweating abnormalities. These autonomic dysfunctions not only intensify neuropathic pain but also impair sensory processing, further complicating symptom presentation and leading to increased discomfort
- Possible chiari malformation (CM): A condition characterized by the downward displacement of the cerebellum, which can co-occur with cervical instability and cranial-cervical junction malformations. Can lead to symptoms such as headaches, neck pain, dizziness, balance problems, swallowing difficulties, sensory disturbances, and nausea
- Possible mild demyelination: Refers to partial damage to the myelin sheath, the protective covering around nerve fibers, which can slow or impair nerve signal transmission, leading to symptoms like weakness, numbness, tingling, and coordination issues, and may be associated with connective tissue disorders that affect nerve function
- Possible sensory processing disorder (SPD): Characterized by hypersensitivity or hyposensitivity to sensory stimuli, difficulty filtering or integrating sensory information, clumsiness, and anxiety or distress in response to specific stimuli. SPD is often linked to neurological dysfunction, including abnormalities in sensory integration and processing, and may be exacerbated by connective tissue-related instability affecting proprioception and sensory perception
- Proprioception issues: Difficulty sensing the body's position in space, leading to impaired spatial awareness, poor coordination, and instability. This dysfunction, caused by disrupted sensory feedback and autonomic regulation, increases the risk of falls or accidents. It is commonly associated with dysfunction in the CNS (central nervous system) or PNS (peripheral nervous system)
- Pupil dilation or constriction abnormalities: Reflecting autonomic nervous system (ANS) dysfunction, particularly affecting the eye's ability to adjust to light due to dysregulation of the pupillary reflex
- Raindrop sensations: Caused by sensory disturbances, often linked to nerve or autonomic dysfunction, where abnormal nerve signaling leads to sensations resembling the feeling of raindrops or light touches on the skin
- Sensitivity to touch: Heightened tactile sensitivity, often a manifestation of neuropathy or central sensitization, leading to discomfort or pain from normally innocuous stimuli
- Sensory processing issues: Difficulty integrating and responding to sensory input, often associated with neurological dysregulation or central nervous system (CNS) dysfunction. This can include sensory overload in crowded places, where heightened stimuli—such as noise, light, and movement—overwhelm the nervous system, leading to feelings of anxiety, dizziness, or

irritability. These challenges can make it difficult to tolerate everyday environments, particularly those with multiple sensory inputs

- Skin crawling feeling: Often linked to small fiber neuropathy (SFN) or autonomic dysfunction, this sensation can result from neurological disturbances, where connective tissue issues affect nerve function and sensory processing
- Slowed reaction times, due to impaired neural signal transmission
- Soft tissue injuries: Due to connective tissue fragility, individuals may experience frequent strains, sprains, and tears, which contribute to muscular dysfunction and delayed recovery
- Speech difficulties: Including word-finding problems (e.g., the “tip-of-the-tongue phenomenon”), often due to cognitive dysfunction, neurological impairment, or autonomic dysregulation
- Tremors and myoclonus: Neurological instability and motor dysfunction may lead to involuntary movements such as tremors or myoclonus (sudden jerking movements), which may be exacerbated by autonomic dysregulation or muscle weakness
- Vagus nerve involvement: Affecting multiple autonomic functions, including heart rate, digestion, and respiratory control, contributing to dysautonomia and autonomic dysfunction
- Variability in symptoms: Fluctuating severity and intensity of neurological manifestations, often due to the unpredictable nature of autonomic dysfunction and connective tissue instability
- Vertigo or dizziness: Often related to vestibular dysfunction, autonomic instability, or neurological issues affecting balance and spatial orientation
- Vestibular dysfunction: Dysfunction in the vestibular system (the part of the inner ear and brain that controls balance) is common, leading to symptoms such as dizziness, vertigo, imbalance, or motion sensitivity, often exacerbated by autonomic dysfunction
- Weakness or numbness in limbs: Commonly associated with motor neuropathy, peripheral nerve involvement, or central neurological dysfunction affecting muscle strength and sensation
- Word-finding difficulties: Difficulty recalling words or names, often associated with cognitive dysfunction, memory impairment, or neurological involvement

Neuromuscular (NM) System Symptoms:

- Ataxia: Impaired coordination affecting balance, gait, and posture, resulting from joint instability, proprioceptive dysfunction, and muscle weakness
- Cervical instability: Resulting from connective tissue laxity, hypermobility, and ligamentous insufficiency, leading to inadequate stabilization of the cervical spine. This causes excessive movement, misalignments, nerve compression, spinal cord irritation, and neurological deficits such as radiculopathy, sensory disturbances, muscle weakness, and neck pain. Symptoms also include occipital headaches, chronic neck pain, stiffness, limited range of motion, and neurological symptoms like numbness, tingling, and weakness, with potential involvement of the upper limbs
- Coordination difficulties: Impaired motor control and balance resulting from neurological or muscular dysfunction, muscle weakness, and proprioceptive impairments
- Delayed muscle recovery: Characterized by prolonged fatigue and reduced ability to recover post-exercise, often linked to neuromuscular instability and hypermobility
- Difficulty with fine motor skills: Challenges in tasks requiring dexterity and precision due to impaired muscle function and joint instability

- Frequent falls: Often resulting from impaired balance, muscle weakness, proprioceptive impairments, and joint instability
- Dissociation: A neurological phenomenon involving detachment from reality, often due to overwhelming sensory input or autonomic dysregulation, leading to emotional numbness or detachment from one's body or surroundings
- Hand tremors: Due to autonomic dysfunction, joint instability, neuropathy, muscle weakness, and CNS dysfunction
- Impaired fine motor control and hand weakness: Often due to neuropathic conditions, including peripheral neuropathy or central nervous system dysfunction, affecting dexterity and coordination
- Increased fatigue after mental exertion: Due to cognitive overload from hypermobility-related instability and autonomic dysfunction
- Muscle atrophy: Muscle wasting or weakening over time due to chronic disuse, neuromuscular dysfunction, or impaired muscle activation
- Muscle cramps and spasms: Sudden, involuntary, and often painful contractions of skeletal muscles, commonly seen in hypermobility syndromes and musculoskeletal dysfunction. These can result from neuromuscular dysfunction, joint instability, and abnormal muscle activation and tension. Muscle spasms, in particular, are often due to joint instability and neuromuscular dysfunction, leading to irregular muscle activation and tension
- Muscle fatigue: Caused by sustained activity or underlying neuromuscular instability, resulting in early exhaustion, reduced endurance, and difficulty recovering from physical exertion
- Muscle stiffness: Marked by increased muscle tone or resistance to passive movement, indicative of neuromuscular dysfunction, often mistaken for spasticity but primarily caused by instability in hypermobile joints and connective tissues
- Muscle weakness: A reduction in strength that leads to difficulty performing physical tasks, often exacerbated by joint instability and ligament laxity
- Neurogenic bladder symptoms: Bladder dysfunction due to autonomic nervous system involvement, causing difficulty with urinary retention, urgency, frequency, or incontinence
- Neuropathy and neuropathic pain: Peripheral neuropathy leading to burning, shooting pain, tingling, numbness, or weakness, typically linked to nerve damage, compression, or dysfunction in the peripheral nervous system
- Reduced stamina: Characterized by decreased endurance and early fatigue during physical activity, resulting from muscular dysfunction and inefficient energy use due to connective tissue abnormalities
- Sensation of heaviness in limbs: Often related to muscle weakness, neuromuscular dysfunction, or circulatory impairment associated with hypermobility
- Tremors and myoclonus: Neurological instability and motor dysfunction manifest as rhythmic muscle contractions, leading to involuntary movements such as tremors (shaking or oscillation) or myoclonus (sudden, jerking movements). These symptoms are often a response to mechanical instability or arise as secondary effects of joint dislocations and neurological dysfunction. They are frequently exacerbated by autonomic dysregulation and muscle weakness, further compounding the clinical presentation
- Weak grip strength: Often resulting from reduced muscle tone, instability, or neuromuscular dysfunction in the hands, affecting dexterity and making tasks requiring fine motor skills more difficult

Neurovascular System Symptoms:

- Possible popliteal entrapment syndrome: A condition where the popliteal artery is compressed, leading to reduced blood flow to the lower leg. Symptoms include calf pain, cramping, numbness, and cold feet, especially during exercise
- Possible thoracic outlet syndrome (TOS): A condition caused by compression of nerves or blood vessels in the thoracic outlet, the space between the collarbone and first rib. This compression can lead to neurological symptoms such as pain in the shoulders, neck, arms, and hands, numbness, tingling in the fingers, and a weakened grip, along with potential vascular symptoms like swelling or coldness in the arms

Oral Symptoms:

- Chronic dry mouth (xerostomia): A persistent reduction in saliva production due to autonomic dysfunction, connective tissue abnormalities, or medication side effects. This leads to recurrent dry mouth, contributing to difficulty swallowing, increased risk of dental decay, gum disease, oral infections, and overall oral discomfort
- Crimson crescents: Red, visible lines or indentations along the gum line, typically near the skin flaps of the mouth. These are often linked to connective tissue laxity, vascular changes, and gum hypermobility. They can also indicate connective tissue weakness and are sometimes associated with chronic fatigue. Inflammation of the gums can exacerbate their appearance, contributing to oral discomfort
- Dental crowding: Due to abnormal collagen production and connective tissue laxity, this can lead to misalignment of the jaw and insufficient space for teeth. Wisdom teeth extraction is common for this reason
- Dental issues: Individuals often experience various dental problems, including increased susceptibility to tooth enamel erosion due to soft tissue laxity and impaired tissue regeneration
- Delayed or poor wound healing in the mouth: Due to connective tissue dysfunction, cuts, oral surgeries, or dental extractions may take longer to heal, leading to increased risk of infection or other complications
- Difficulty swallowing (dysphagia): Often caused by muscle weakness, jaw instability, or neurological dysfunction affecting the muscles responsible for swallowing. This can be exacerbated by autonomic dysregulation or esophageal motility issues
- Discomfort while chewing: Possibly due to joint instability in the TMJ or muscle weakness in the jaw
- Dry or cracked lips: Due to reduced saliva production (xerostomia) or compromised skin elasticity, individuals may develop dry or cracked lips, especially around the corners of the mouth
- Excessive salivation: In some cases, individuals may experience excessive saliva production due to impaired swallowing or difficulties with mouth closure, which can lead to drooling
- Gum sensitivity and fragility: Hyperelasticity and vascular fragility of the gums, resulting in pain, irritation, or bleeding even with minimal pressure or brushing
- High palate: Due to craniofacial abnormalities and connective tissue laxity, individuals may have a high, arched palate, which can contribute to dental malocclusion or airway problems

- Jaw instability or misalignment: Hypermobility in the temporomandibular joint (TMJ) can lead to jaw misalignment, pain, and difficulty with chewing or speaking, often exacerbated by joint instability
- Oral abrasions or sensitivity: Oral mucosal fragility and tissue laxity can result in abrasions, cuts, or increased sensitivity in the mouth, especially during eating or speaking
- Oral sensitivity to temperature: Heightened sensitivity of the oral mucosa and dental enamel to hot or cold temperatures, possibly linked to nerve involvement or dysregulated blood flow
- Oral ulcers, mucosal fragility, or desquamation, including conditions such as canker sores (aphthous ulcers) and stringy skin peeling of the oral mucosa
- Smaller mouth size, due to connective tissue abnormalities, is related to collagen dysfunction, which affects the growth and alignment of the jaw and facial bones
- Speech difficulties: Due to jaw instability, temporomandibular joint (TMJ) dysfunction, and soft tissue laxity, individuals may experience difficulty articulating words, slurred speech, or increased fatigue during speaking
- Temporomandibular joint (TMJ) dysfunction: Instability in the TMJ due to hyperelastic ligaments and joint laxity can result in pain, clicking, grating sounds, limited jaw movement, and headaches
- Tooth decay: Soft enamel and increased salivary dysfunction (from xerostomia) contribute to a higher risk of tooth decay, cavities, and dental erosion
- Worn-down teeth: Bruxism (teeth grinding), often seen in individuals with TMJ dysfunction and muscle weakness, leads to tooth wear, fractures, or misalignment over time
- Wiggly or loose adult teeth: The hypermobility and soft tissue laxity can result in loose teeth or teeth that wiggle, due to weakened ligaments and supporting structures, increasing the risk of premature tooth loss

Psychological Symptoms:

- Cognitive frustration: Impaired concentration, memory, and mental clarity due to chronic pain, fatigue, and cognitive fog, leading to frustration, feelings of inadequacy, and exacerbating stress and anxiety
- Emotional lability: Heightened emotional responses, such as irritability, mood swings, anxiety, panic attacks, social anxiety, and a pervasive sense of doom, often resulting from chronic pain, fatigue, and physical limitations. This includes grief and emotional exhaustion due to persistent fatigue and the need for frequent rest
- Existential anxiety: Anxiety related to long-term uncertainty of health outcomes, encompassing concerns about disease progression, disability, and quality of life
- Grief and identity struggles: Feelings of loss due to the inability to perform previously manageable tasks or maintain a "normal" life, leading to grief, guilt, and a loss of self-identity. This emotional burden can contribute to isolation and difficulty adapting to a new reality
- Health anxiety: Persistent concern over physical symptoms, potential flare-ups, and disease progression. This anxiety is compounded by frequent medical appointments, diagnostic testing, and the uncertainty surrounding long-term outcomes
- Sense of loss of control: The unpredictable nature of the condition leads to a psychological sense of powerlessness, as physical instability, pain, and other symptoms disrupt daily life, undermining the ability to maintain control over one's body and routines

- Social withdrawal: Physical limitations, such as joint pain and fatigue, often lead to isolation. The fear of being misunderstood or judged can further discourage social interaction

Renal/Kidney and Urogenital System Symptoms:

- Chronic kidney pain: Persistent discomfort localized to the kidneys, potentially linked to connective tissue disorders, which may affect renal parenchymal integrity or surrounding structures. This can lead to structural or functional changes in the kidneys, resulting in pain or discomfort
- Decreased renal function: Impaired renal function due to connective tissue dysfunction, potentially causing structural abnormalities in the kidneys (e.g., alterations in the renal vasculature, tubules, or glomeruli). This dysfunction can disrupt filtration processes, leading to the accumulation of waste products (e.g., urea, creatinine) in the bloodstream
- Glomerular filtration rate (GFR) abnormalities: Abnormalities in GFR, often due to connective tissue-related weakening of the glomerular basement membrane or vasculature, compromising renal filtration. This can result in impaired blood filtration, potentially causing fluid retention, electrolyte imbalances, or uremia due to inefficient clearance of waste products
- Hydration imbalance: Difficulty maintaining fluid balance due to dysautonomia or renal dysfunction, leading to either dehydration or fluid retention. Impaired autonomic regulation disrupts the kidneys' ability to manage fluid homeostasis, exacerbating issues like blood pressure dysregulation, edema, or dehydration, especially in the context of connective tissue abnormalities
- Incontinence: Involuntary bladder control loss due to pelvic floor dysfunction, autonomic nervous system dysregulation, or nerve involvement. Connective tissue abnormalities may weaken the muscles, ligaments, and nerves controlling the bladder, resulting in urinary incontinence, urgency, or overflow incontinence
- Nocturia (frequent urination): Increased urination frequency at night, often associated with dysautonomia, fluid retention, and circadian rhythm disruption. Impaired renal function or autonomic dysregulation can lead to abnormal fluid regulation, causing nocturnal polyuria or frequent awakenings to urinate during sleep
- Urogenital manifestations: Result from connective tissue abnormalities affecting the strength and elasticity of tissues in the urinary and reproductive systems. These include urinary incontinence (difficulty holding urine, leakage under stress, urgency, and frequency), pelvic floor dysfunction (weakness leading to prolapse, incontinence, and pelvic pain, especially with prolonged sitting or standing), bladder issues (overactive bladder, incomplete bladder emptying, retention, or difficulty starting a stream), sexual dysfunction (pain during intercourse due to pelvic hypermobility and tissue fragility, reduced elasticity causing discomfort), and reproductive organ involvement (pelvic pain due to ligament laxity, abnormal menstrual cycles, endometriosis, and an increased risk of miscarriage or pregnancy complications due to weakened connective tissue supporting the uterus)

Skin/Dermatological Symptoms:

- Abnormal scarring patterns or excessive scarring: Due to impaired collagen formation, leading to hypertrophic or keloid scars from connective tissue dysfunction

- Bruising easily: More frequent or severe bruising due to weakened blood vessel walls and impaired collagen production
- Capillary fragility: Increased tendency for capillaries to rupture with minimal pressure, leading to visible spots or bruising on the skin
- Chronic pruritus: Persistent itching, often linked to skin fragility, neurovascular dysregulation, or mast cell activation, resulting in heightened sensitivity and discomfort
- Dark circles: Caused by thinner, more translucent skin due to connective tissue abnormalities, making blood vessels under the eyes more visible. Poor circulation, frequent fatigue, and easy bruising can also contribute to their appearance. Genetics may further influence the severity of dark circles
- Delayed wound healing: Impaired collagen synthesis and connective tissue dysfunction slow tissue repair, extending recovery times
- Dermographia (skin writing, dermatographism, or dermatographism): Raised red lines or welts appear on the skin following scratching or pressure, reflecting hypersensitivity of both the skin and vasculature. This is often linked to vascular fragility and neurovascular dysregulation, where the skin and blood vessels react abnormally to mechanical stimuli, resulting in visible skin changes. It may also be associated with mast cell activation, histamine release, or connective tissue abnormalities affecting vascular integrity
- Easy skin tearing: Due to reduced collagen strength and connective tissue support, skin becomes more prone to spontaneous lacerations or tears with minimal trauma
- Frequent rashes or hives: Common in individuals with mast cell activation syndrome (MCAS), often presenting as raised, red, itchy patches or welts
- Hyperpigmentation or hypopigmentation: Areas of increased or decreased pigmentation due to the skin's impaired healing ability or abnormal melanocyte function
- Increased skin and eye sensitivity to sunlight: Compromised skin barrier function and vascular fragility lead to increased sensitivity to UV radiation, causing quicker sunburns or rashes
- Loss of skin turgor: Reduced skin elasticity or tone, which may result in the skin appearing loose or saggy, especially in the face or neck area
- Mild skin hyperextensibility or hyperelasticity: Skin that stretches more than typical due to abnormal connective tissue, often presenting as loose or easily stretched skin (hyperelastic)
- More prone to imprints and marks due to underlying connective tissue abnormalities
- Recurrent minor cystic lesions (hEDS): Small, often asymptomatic epidermoid or pilosebaceous cysts that recur due to dermal fragility and compromised connective-tissue integrity characteristic of hEDS. Weakened extracellular matrix and defective collagen within the dermis reduce structural support for pilosebaceous units, predisposing to formation of cystic lesions, slow resolution, and recurrence. These lesions are typically non-painful unless manipulated and may be associated with subtle surrounding skin vulnerability, reflecting systemic connective-tissue fragility manifesting in cutaneous structures
- Seborrheic dermatitis: A chronic inflammatory skin condition causing flaky, scaly patches, often found on the scalp or face, which could be linked to immune system dysregulation
- Skin fragility: The skin becomes more vulnerable to damage, tearing, or bruising from minor trauma due to compromised connective tissue support and reduced collagen
- Skin laxity: Loose, hyperelastic, skin caused by defects in collagen or connective tissue fibers, leading to skin that easily stretches and sags
- Soft, velvety skin: A soft, smooth texture due to connective tissue abnormalities affecting the dermis, despite underlying skin fragility

- Thin, translucent skin: The skin may appear paper-thin, especially around the hands, arms, or other areas, due to the lack of collagen support

Vascular (VS) System Symptoms:

- Abnormal heart rhythms (arrhythmias): Resulting from autonomic dysregulation and impaired vascular tone, disrupting typical electrical heart activity
- Adverse reactions to weather changes: Sensitivity to temperature and humidity fluctuations due to autonomic dysfunction and impaired vascular response, causing discomfort or exacerbating symptoms
- Aortic root dilation (vascular/connective-tissue): Pathologic enlargement of the proximal ascending aorta at the level of the aortic root, resulting from structural weakness of the aortic wall secondary to connective-tissue abnormalities, including defective collagen and extracellular matrix integrity characteristic of hEDS. This dilation may compromise aortic valve function, predispose to aortic regurgitation, and increase the risk of progressive aneurysmal expansion or dissection. Hemodynamic stress, reduced aortic wall tensile strength, and intrinsic vascular fragility contribute to long-term cardiovascular complications, warranting serial imaging surveillance and risk stratification
- Dermatographia: Also known as dermographia or dermatographism, this condition causes raised, red lines to appear where the skin is lightly scratched. It is a type of physical urticaria (hives) and is generally harmless and temporary, though it can be uncomfortable. The reaction occurs due to an exaggerated immune response, releasing histamine and resulting in raised welts
- Dilated veins: Venous enlargement from venous insufficiency or vascular fragility, leading to visible varicosities or blood pooling in the extremities
- Discoloration of extremities: Changes in skin color (red, blue, purple, white) from impaired circulation or vascular instability, indicating reduced blood flow or vascular constriction
- Dysautonomia: It affects blood flow by disrupting the autonomic nervous system's control over blood pressure and heart rate, leading to issues like orthostatic intolerance. This can worsen vascular complications due to already fragile blood vessels
- Fragile skin: Due to defects in collagen production, the skin becomes more prone to bruising, tearing, and scarring. This fragility extends to blood vessels as well
- Increased frequency of bruising: Fragile blood vessels and compromised vascular integrity contribute to spontaneous bruising, especially with minor impact
- Increased susceptibility to livedo reticularis (LR): A net-like skin pattern indicating impaired circulation or vascular instability, with individuals showing greater susceptibility to LR due to underlying vascular fragility
- Interstitial fluid balance abnormalities (connective-tissue): Dysregulation of fluid distribution between the intravascular and interstitial compartments resulting from connective-tissue fragility, altered extracellular matrix composition, and impaired lymphatic or vascular support characteristic of hEDS. Compromised vessel wall integrity, reduced tissue tensile strength, and dysfunctional lymphatic drainage can lead to abnormal interstitial fluid accumulation, localized edema, or impaired tissue perfusion. Clinically, these abnormalities may contribute to swelling of extremities, postural fluid shifts, orthostatic intolerance, and secondary strain on musculoskeletal structures, reflecting the systemic impact of connective-tissue weakness on vascular and interstitial homeostasis

- Mucocutaneous bleeding tendency (gingival bleeding): Increased propensity for spontaneous or trauma-induced bleeding of the gingiva, reflecting underlying connective-tissue fragility and vascular wall weakness characteristic of hEDS. Defective collagen and extracellular matrix integrity in small-caliber blood vessels and supporting periodontal structures compromises vessel stability, predisposing to easy capillary rupture, prolonged bleeding, and delayed hemostasis. Clinically, this may manifest as bleeding with minimal mechanical stress (e.g., toothbrushing, chewing) and may co-occur with other mucocutaneous hemorrhagic features
- Orthostatic intolerance: Difficulty standing for prolonged periods due to blood pooling in the lower extremities and impaired vascular tone, which can exacerbate symptoms of dizziness, lightheadedness, or fainting. This condition is related to the vascular fragility and compromised autonomic control. Impaired vascular tone leads to poor blood flow regulation and venous insufficiency, making it difficult to maintain circulation while standing. This can lead to pooling of blood in the legs, reduced blood return to the heart, and increased symptoms of fatigue and dizziness, especially with postural changes
- Periorbital hyperpigmentation: Dark circles under the eyes due to vascular fragility and poor circulation, often exacerbated by chronic fatigue or sleep disturbances
- Pelvic congestion syndrome: Chronic pelvic pain caused by the enlargement of veins in the pelvis (pelvic varices), which can lead to symptoms such as lower abdominal pain and a sensation of fullness in the pelvic area
- Possible median arcuate ligament syndrome (MALS): A condition where the median arcuate ligament compresses the celiac artery, leading to reduced blood flow to the abdominal organs. Symptoms include abdominal pain (especially after eating), weight loss, nausea, and vomiting
- Possible superior mesenteric artery syndrome (SMAS): A rare condition where the duodenum (the first part of the small intestine) is compressed between the abdominal aorta and the superior mesenteric artery. Symptoms include severe abdominal pain, nausea, vomiting, and significant weight loss due to difficulty in food passage through the duodenum.
- Postural hypotension: Low blood pressure upon standing, which may occur due to vascular instability and autonomic dysfunction, leading to dizziness or fainting
- Spontaneous bleeding: Any form of unexplained bleeding, such as nosebleeds or gum bleeds, would be a hematological manifestation of vascular fragility or clotting issues
- Spontaneous bruising or skin tears: Increased vascular fragility leads to blood vessel rupture or leak and unexplained bruising with minimal impact or trauma
- Temperature sensitivity in extremities: Impaired vascular regulation and autonomic dysfunction causing heightened sensitivity to temperature, especially in extremities
- Vascular compressions: Conditions where blood vessels are compressed, resulting in impaired circulation and potential ischemia. These can lead to symptoms such as pain, swelling, and compromised organ function. Examples include MALS, SMAS, and May-Thurner syndrome. Vascular compression syndromes are often observed in individuals with connective tissue disorders and dysautonomia due to the structural weakness of blood vessels and their susceptibility to compression
- Vascular fragility and skin sensitivity: Weak blood vessels, vascular fragility, and increased susceptibility to spontaneous bleeding, and easy bruising
- Venous insufficiency: Poor blood return from extremities, causing swelling (edema), varicose veins, and skin texture or color changes, particularly in the lower legs

Vestibular/ENT System Symptoms:

- Dizziness, balance disturbances, or vertigo: These symptoms may arise from vestibular dysfunction, often associated with impairments in the mechanoreceptors and proprioception of the inner ear. Autonomic dysregulation, including compromised cerebral blood flow and altered neural signaling, can further exacerbate vestibular symptoms, leading to dizziness, vertigo, and balance disturbances
- Eustachian tube dysfunction (ETD): A condition in which the Eustachian tube, connecting the middle ear to the nasopharynx, fails to regulate air pressure and fluid drainage properly. This dysfunction can cause symptoms such as a sensation of ear fullness, muffled hearing, tinnitus, and discomfort, including ear pain or popping. Connective tissue abnormalities, particularly in hypermobile individuals, may weaken the structural integrity of the Eustachian tube, further compromising its function and exacerbating these symptoms
- Possible semicircular canal dehiscence (SCD): A pathological condition characterized by a dehiscence or abnormal thinning of the bone encasing one or more of the semicircular canals in the inner ear. This condition may result in abnormal communication between the inner ear and the cranial cavity, leading to symptoms such as autophony (amplification of internal sounds), fluctuating conductive hearing loss, pressure-sensitive vertigo, imbalance, and tinnitus. These symptoms are attributed to disturbed sound conduction and altered vestibular input caused by the dehiscence, which disrupts normal vestibular system function
- Vestibular dysfunction: A disorder of the vestibular system, responsible for maintaining balance and spatial orientation. Autonomic dysfunction can impair blood flow to the inner ear, disrupting normal vestibular processes. This can manifest as symptoms including dizziness, vertigo, imbalance, spatial disorientation, nystagmus (involuntary, repetitive eye movements), blurred vision, motion sensitivity, fatigue, cognitive impairment, difficulty tracking moving objects, tinnitus, and headaches. The interplay between autonomic dysregulation and vestibular dysfunction contributes to the broad spectrum of sensory and motor disturbances observed in these conditions

Visual Symptoms:

- Astigmatism: A refractive error caused by an irregular curvature of the cornea or lens, leading to distorted or blurred vision. This condition can progressively worsen over time, and the visual distortion is typically due to the unequal focusing of light rays on the retina, causing reduced visual clarity and difficulty seeing fine details
- Binocular vision dysfunction (BVD): This includes double vision (diplopia), eye strain or fatigue, headaches (especially behind the eyes or at the temples), difficulty reading or focusing on objects for extended periods, sensitivity to light, blurred or distorted vision, poor depth perception, and dizziness or vertigo, particularly when reading or looking at screens
- Nearsightedness (myopia): A refractive disorder in which distant objects appear blurry due to the eye's inability to focus light correctly on the retina. This condition is often caused by an elongated eyeball or excessive curvature of the cornea, leading to a progressively increasing prescription for corrective lenses

Vocal Cord Dysfunction (VCD) Symptoms:

- Airway irritation and recurrent laryngitis: This results in chronic hoarseness, loss of voice, sore throat, and a dry cough, often caused by vocal cord inflammation and exacerbated by environmental triggers
- Anxiety-induced exacerbation: VCD symptoms, particularly dyspnea and stridor, can be triggered or worsened by stress, anxiety, or panic, contributing to a vicious cycle of breathing difficulty
- Breathing pattern abnormalities: These include chronic shallow breathing or the use of accessory respiratory muscles, often seen in individuals with VCD as they attempt to compensate for impaired airflow
- Chronic throat clearing: Frequently secondary to airway irritation, postnasal drip, or laryngeal inflammation, it contributes to vocal strain and discomfort. This can also lead to vocal fatigue, hoarseness, and potential laryngeal injury due to excessive irritation
- Dysphagia (difficulty swallowing): This condition carries a heightened risk of aspiration, airway obstruction, or aspiration pneumonia, and often co-occurs with vocal cord dysfunction (VCD) or laryngeal instability
- Dysphonia (hoarseness): This includes vocal alterations such as breathiness, strain, or phonatory disturbances, encompassing issues in quality, pitch, or volume due to laryngeal dysfunction. These issues often involve impaired vocal cord dynamics, with an associated loss of vocal range and endurance
- Dyspnea (air hunger): This occurs with impaired respiratory mechanics and effort, potentially indicating a compromised ability to initiate or sustain breathing. It may also suggest inadequate ventilation or compromised airway patency due to vocal cord dysfunction (VCD)
- Excessive mucosal secretion or post-nasal drip: This can exacerbate airway irritation and increase coughing, throat clearing, or difficulty breathing
- Globus pharyngeus: A sensation of a foreign body, fullness, tightness, or a lump in the throat, often without an identifiable structural cause. It is common in individuals with VCD, reflecting increased sensitivity of the laryngopharyngeal mucosa or muscle tension
- Hyperactive gag reflex: This presents as exaggerated or involuntary throat contraction in response to stimuli, which may complicate swallowing and contribute to the sensation of globus, or the feeling of a foreign body in the throat
- Hyperventilation syndrome: Frequently co-occurring with VCD, this results in symptoms of dizziness, lightheadedness, and further exacerbation of dyspnea
- Impaired inspiratory effort: Characterized by difficulty achieving full and deep inspiration due to respiratory muscle weakness or dysfunction, it is often seen in individuals with VCD, where inspiratory stridor occurs due to paradoxical vocal cord motion during inhalation
- Involuntary adduction of the vocal cords during inspiration: This possibly reflects paradoxical vocal cord motion, obstructing airflow and impairing normal respiration. It contributes to upper airway obstruction and stridor, often misdiagnosed as asthma, exercise-induced asthma, or bronchospasm
- Paroxysmal coughing episodes: Characterized by sudden, intense bouts of coughing, often exacerbated by airway irritation or environmental triggers. These episodes are related to laryngeal hypersensitivity or vocal cord irritation, and they can worsen airway obstruction
- Possible inspiratory stridor: A hallmark of VCD, indicative of obstruction or narrowing of the upper airway. It is often worsened by stress, irritants, or physical exertion

- Upper airway resistance syndrome (UARS): Characterized by increased airway resistance during inspiration, including VCD, which can lead to disrupted sleep patterns, poor oxygenation, and further respiratory complications. It may also cause pale skin, clamminess, or coldness
- Voice fatigue: Characterized by the inability to sustain prolonged vocalization, often resulting from vocal cord or muscle overuse, or laryngeal strain or tension

POTS (Postural Orthostatic Tachycardia Syndrome)

Symptoms

Autonomic Nervous System (ANS) Symptoms:

- Activities that can flare up symptoms like cardiovascular issues (tachycardia, dizziness, presyncope) along with respiratory and sensory disturbances (air hunger, visual changes): Waking up, standing up and walking a few steps, eating, riding in a car, standing, swimming/in a pool, walking, lying in a hammock, lying down, taking a video, walking to the car, walking up stairs, a coughing fit, standing up too quickly, getting up to use the bathroom after a nap, answering a phone call, waiting in line, random nausea and tachycardia, switching the laundry, stretching, drinking water, sneezing, yawning, talking, crying, running a bath in a warm room, laughing hysterically or excessively, lying down for a while then sitting up, sneezing while sitting up, stirring soup, brushing teeth, adjusting/tying hair, preparing food with heat and arm raising, a coughing attack, standing with a headache, exposure to heat, after exercise, dehydration, stress, alcohol, hormonal changes, low blood sugar, prolonged sitting or inactivity, sudden changes in position like bending over or sitting too quickly
- Adrenaline dumps: A response triggered by autonomic dysfunction, where dysregulation of the sympathetic nervous system leads to excessive release of adrenaline (epinephrine) in response to minimal exertion or stress, causing symptoms like tachycardia, anxiety, palpitations, dizziness, headaches, clamminess, sweating, tremors, shortness of breath, chest discomfort, nausea, and fatigue
- Altered heart rate variability: Episodes of tachycardia and palpitations, often triggered by minimal exertion, can present as fluttering or pounding sensations. Arrhythmias like SVT (Supraventricular Tachycardia), VT (Ventricular Tachycardia), bradycardia, and atrial flutter are caused by autonomic dysregulation, leading to irregular electrical impulses. SVT originates in the atria or AV node, where abnormal circuits cause rapid, regular heartbeats, leading to fluttering sensations. Atrial flutter similarly involves the atria, producing rapid but regular beats. VT originates in the ventricles, where abnormal impulses cause rapid, disorganized beats, resulting in pounding sensations. Bradycardia causes slow, irregular rhythms, with occasional forceful beats. These arrhythmias disrupt normal cardiovascular response to exertion or stress
- Altered pain perception: Beyond hyperalgesia, autonomic dysfunction may contribute to a type of "pain amplification" or abnormal pain perception in conditions like fibromyalgia. Individuals may experience burning, tingling, or deep, aching pain that seems to be out of proportion to actual tissue damage
- Altered sweating response: Dysregulated sweating mechanisms, including hyperhidrosis (excessive sweating), hypohidrosis (reduced sweating), or anhidrosis (lack of sweating), which

are often triggered by environmental factors, stress, or exertion. This phenomenon is indicative of autonomic dysfunction affecting the sweat glands' ability to regulate body temperature effectively

- Anxiety and mood dysregulation: Characterized by generalized anxiety, panic attacks, social anxiety, and heightened emotional responses to stressors, exacerbated by autonomic dysregulation and an imbalance in the body's stress response systems. These symptoms are often heightened by sensory overload or environmental triggers
- Autoimmune and inflammatory dysregulation: An increased propensity for autoimmune responses and chronic systemic inflammation, often manifesting in conditions such as joint pain, muscle weakness, and tissue sensitivity. This dysregulated immune response contributes to multisystemic dysfunction, exacerbating other autonomic and musculoskeletal symptoms
- Autoimmune-related skin conditions: While often discussed in terms of musculoskeletal or neurological dysfunction, the autonomic system may also contribute to skin-related issues such as random rashes, or other inflammatory skin responses
- Blood pooling and dependent edema: Accumulation of blood in the lower extremities or abdomen when standing or sitting upright, contributing to swelling, discomfort, or visible venous engorgement
- Blood vessel dilation/constriction abnormalities: Inconsistent blood vessel responses to postural changes, temperature shifts, or exertion can result in exaggerated symptoms like lightheadedness, fainting, or feeling excessively hot or cold
- Checking vitals: Monitoring heart rate, blood pressure, and other vital signs helps track autonomic function and detect issues early
- Chest pain during or after exertion: This is often accompanied by fatigue or breathlessness, and may also occur after meals. It can be associated with conditions affecting the cardiovascular or respiratory systems, including issues like ischemia, vascular dysfunction, or gastrointestinal reflux
- Chronic fatigue and post-exertional malaise: The profound, prolonged fatigue and malaise that follows exertion (even minimal) may not always be linked to cardiovascular instability but is often tied to the body's inability to recover from autonomic dysregulation. This is distinct from typical "cardiac" fatigue and relates more to systemic energy dysregulation
- Chronic low blood sugar (hypoglycemia): Inconsistent regulation of blood sugar due to autonomic dysfunction, leading to fatigue and irritability
- Chronic thirst and frequent urination: Symptoms that may mimic diabetes insipidus due to dysregulation of ADH (antidiuretic hormone), affecting water retention
- Cold shivers or full-body jerks: Cold shivers, or thermoregulatory shivering, are a response to your body trying to generate heat when it senses cold. This can be exacerbated by the body's inability to properly regulate blood flow and temperature, leading to more pronounced or frequent shivering. Additionally, full-body jerks or myoclonus can occur as involuntary muscle movements or spasms in response to cold or other triggers
- Cognitive dysfunction, decline, "dementia-like" symptoms, and mental fatigue: Marked by cognitive impairments such as memory deficits, brain fog, difficulty concentrating, and impaired executive function. These symptoms often worsen post-exertion, postprandially, or following stress, leading to profound fatigue, post-exercise malaise, and diminished mental clarity. Cognitive overload may trigger emotional dysregulation, panic, or difficulty processing information, impairing social and professional interactions. Brain fog and memory problems could extend into more severe cognitive impairment in some individuals, mimicking early-stage

dementia due to poor cerebral blood flow, neurotransmitter imbalances, and autonomic dysfunction affecting neurovascular health

- Compression garments: Improve venous return and prevent blood from pooling in the lower extremities. They are often used to help manage blood pooling, improve circulation, and support venous return, especially in individuals with autonomic issues like orthostatic intolerance or dysautonomia
- Cystic fibrosis-like symptoms (CF): In some cases, individuals may experience altered mucus production, which can be excessive or limited, leading to respiratory issues such as chronic cough, difficulty breathing, and increased susceptibility to infections
- Delayed gastric emptying: Often tied to nausea, vomiting, or a feeling of fullness, even after small meals, which can worsen autonomic and gastrointestinal symptoms
- Dehydration and electrolyte imbalances: Chronic dehydration despite fluid intake, coupled with imbalanced electrolyte levels like low sodium or potassium, may lead to dizziness, fatigue, and muscle cramps
- Derealization and dissociation: Episodes of derealization and dissociation, often triggered by sensory overload, autonomic instability, or emotional stress. These symptoms can cause feelings of detachment from reality, confusion, and difficulty maintaining a coherent sense of self during stress or exhaustion
- Dysregulated salivary glands: This includes excessive salivation (hypersalivation), dry mouth (xerostomia), and difficulty swallowing (dysphagia), with fluctuations between these extremes depending on autonomic changes, particularly during vasodilation or stress responses
- Dysregulated tear ducts: This includes excessive tearing (epiphora), dry eyes (keratoconjunctivitis sicca), tearing due to light sensitivity (photophobia), and increased emotional tearing or crying, varying based on autonomic fluctuations and sensory stimuli such as bright light or stress
- Emotional dysregulation and lability:
Marked by mood swings, emotional numbness, irritability, and heightened stress responses to triggers. These symptoms are often worsened by autonomic nervous system dysregulation, impairing emotional regulation and leading to overwhelm or exhaustion from daily tasks or social interactions. This instability frequently contributes to feelings of panic and difficulty managing stress responses
- Exercise intolerance: Severe fatigue or dizziness triggered by exercise, often resulting in PEM (post-exertional malaise), even after minimal physical activity. Individuals with dysautonomia may also experience a heightened drop in blood pressure or increased heart rate during exercise, leading to fatigue, dizziness, or fainting
- Exercise-induced hypotension: While orthostatic hypotension is common, some individuals may experience a drop in blood pressure during exercise (exercise-induced hypotension), which could lead to dizziness, fatigue, or fainting episodes following physical activity
- Facial flushing: Associated with dysregulation of the ANS (autonomic nervous system), particularly in the sympathetic and parasympathetic control of vascular tone. Dysfunction in these pathways can lead to abnormal vasodilation of cutaneous blood vessels, resulting in increased blood flow to the skin and the appearance of flushing
- Feeling your pulse in your whole body: Sensitivity to blood flow or heightened awareness of circulatory dynamics, possibly indicative of autonomic dysregulation or increased sympathetic nervous system activity often seen in conditions like dysautonomia

- Frequent hunger, gastrointestinal dysregulation, and malabsorption: Characterized by frequent hunger, bloating, dysphagia (difficulty swallowing), and motility issues like gastroparesis, constipation, and diarrhea. These symptoms result from impaired gastrointestinal function and reduced absorption of nutrients, electrolytes, and water, leading to dehydration, nutrient deficiencies, and gastrointestinal discomfort. The unpredictability of these symptoms can contribute to emetophobia (the fear of vomiting), as individuals may develop a heightened anxiety about the possibility of nausea or vomiting, especially when digestive issues are frequent and unpredictable
- Frequent hydration: Helps manage blood volume and improve circulation
- Gastrointestinal dysmotility and related syndromes: Conditions like gastroparesis, and slow-transit constipation are common, with symptoms including bloating, nausea, vomiting, abdominal pain, early satiety, and fluctuating bowel habits. These result from impaired autonomic control of the enteric nervous system
- Histamine intolerance: This can contribute to symptoms such as dizziness, heart palpitations, fatigue, and lightheadedness, which are already common in autonomic dysfunction. Histamine release may also exacerbate symptoms like flushing, nasal congestion, and headaches, with histamine-related flushing sometimes triggering an exaggerated autonomic response, leading to increased heart rate, dizziness upon standing, and worsening fatigue. These reactions can occur when histamine isn't efficiently broken down, intensifying the autonomic instability
- Hormonal dysregulation: Hormones like aldosterone, antidiuretic hormone (ADH), norepinephrine, dopamine, renin, and cortisol may not function properly, leading to issues with fluid retention, electrolyte balance, and blood pressure regulation, all of which worsen orthostatic intolerance
- Hyperadrenergic state: A heightened sympathetic nervous system response with excessive release of norepinephrine and other catecholamines. This leads to symptoms such as tachycardia, hypertension, anxiety, tremors, sweating, and palpitations, often triggered by minimal exertion or stress
- Hypermetabolic state: This can manifest as unexplained weight loss, increased appetite, or an inability to maintain body weight. This dysregulated energy balance is often overlooked and may be tied to autonomic dysfunction, particularly involving the sympathetic nervous system or hypothalamic-pituitary-adrenal (HPA) axis or thyroid function
- Impaired thermogenesis and hunger regulation: Beyond the typical thermoregulatory dysfunction, there can be changes in appetite regulation and satiety signaling. Some individuals experience cravings for high-calorie foods or an inability to regulate appetite properly due to hypothalamic dysfunction associated with autonomic imbalance
- Increased sensitivity to environmental changes: This refers to heightened responsiveness to factors such as temperature fluctuations, humidity, air quality, or environmental stressors, often leading to exacerbated symptoms or discomfort, particularly in individuals with autonomic dysfunction or conditions like VCD (vocal cord dysfunction)
- Internal and external shakiness: Linked to dysautonomia, where autonomic dysfunction affects blood flow and muscle control, leading to both internal trembling (a sensation of shakiness) and external tremors (visible shaking of limbs)
- Medication and salt tablets: Used to increase blood volume and blood pressure to counteract low blood pressure and improve circulation
- Motor dysfunction: Characterized by gait instability, poor coordination, and tremors, often due to neuromuscular impairments, autonomic dysregulation, and poor blood flow. Hypotonia (low

muscle tone) contributes to instability, balance issues, and difficulty performing fine motor tasks. Issues like muscle weakness are frequently seen in those with hypermobility or autonomic dysfunction, often exacerbating balance and mobility challenges

- Musculoskeletal and pain syndromes: Musculoskeletal pain, hyperalgesia (increased pain sensitivity), and myalgia (muscle pain) often exacerbated by circulatory instability, autonomic dysfunction, and muscle weakness. These symptoms may involve widespread pain and heightened sensitivity to stimuli, leading to significant discomfort

- Neurogenic bladder or bladder dysfunction: This involves incomplete emptying of urinary retention due to impaired autonomic control of detrusor muscle contraction and sphincter relaxation. Disrupted parasympathetic and sympathetic coordination leads to abnormal bladder storage and voiding

- Neurological and sensory dysfunction: Symptoms include paresthesia (numbness, tingling), sensory hypersensitivity (e.g., photophobia, hyperacusis), and heightened sensitivity to environmental stimuli (e.g., light, sound, temperature), often due to disrupted sensory processing and autonomic dysfunction. Hyperalgesia and other sensory disturbances may further complicate daily functioning

- Neurotransmitter dysregulation: Influenced by changes in the body's stress response, cardiovascular regulation, and hormonal balance. Imbalances in key neurotransmitters such as norepinephrine, dopamine, serotonin, and acetylcholine can lead to symptoms like mood swings, anxiety, brain fog, and difficulty concentrating. Additionally, adrenaline dumps—often triggered by standing or stress—can cause heightened anxiety, rapid heart rate, dizziness, and a feeling of being overwhelmed. These issues are often exacerbated by cardiovascular instability and hormonal irregularities, further intensifying the challenges with mental clarity, emotional stability, and overall cognitive function. Norepinephrine plays a crucial role in the stress response, regulating alertness and arousal; imbalances can cause heightened anxiety, rapid heart rate, and poor concentration. Dopamine controls mood, motivation, and reward; dysregulation can lead to low energy, lack of motivation, apathy, and cognitive fog. Serotonin is essential for mental health, regulating mood, sleep, and appetite; low levels are linked to depression, anxiety, and sleep disturbances. Acetylcholine is key for memory, learning, and muscle activation; imbalances can lead to cognitive decline, memory issues, and muscle weakness, and it also plays a role in heart rate regulation

- Neurovascular instability: Underpinning cognitive dysfunction, headaches, and dizziness

- Nutrient deficiencies and malabsorption: The dysregulation of the autonomic nervous system, particularly the enteric system, may contribute to GI motility disorders, which in turn can cause nutrient malabsorption, leading to deficiencies in vitamins and minerals, especially vitamin D, B12, and iron

- Ocular dysautonomia: A disorder characterized by visual disturbances resulting from autonomic dysfunction, including blurred vision, difficulty focusing, eye fatigue, glare sensitivity, and impaired light adaptation. It may present with visual blackouts, ocular pain with eye movement, and symptoms such as dry eyes (insufficient tear production, irritation, grittiness), photophobia, pupil abnormalities (anisocoria, sluggish or irregular light responses), difficulty adjusting to light, diplopia, and trouble with eye movements (tracking objects or quick gaze shifts). Additionally, it can cause tearing issues (excessive or insufficient tear production), blurry vision or visual blackouts with postural changes, and eye discomfort

- Orthostatic intolerance: Characterized by dizziness, lightheadedness, and syncope upon standing, this condition is exacerbated by impaired cardiovascular responses and compromised

venous return. Symptoms are often triggered or worsened by physical exertion, sudden postural changes, and prolonged head movements or extended standing, leading to dizziness due to compromised autonomic regulation and impaired blood flow to the brain. Related symptoms include a sensation of increased gravitational pull, often felt as if gravity is pulling harder, which can result from dysautonomia, poor blood circulation, or issues with blood volume regulation. Propping feet up for circulation is common to assist venous return. Blood pooling, where blood accumulates in the lower extremities due to gravitational forces, can impair effective venous return and exacerbate these symptoms during prolonged standing, postural changes, or sudden movements. Reaching up high and bending over can also flare symptoms due to positional changes affecting blood pressure and circulation, further aggravating these responses. Increased chances of urination syncope, linked to autonomic dysfunction and specifically vagal responses, can also contribute to these effects

- Orthostatic tachycardia: An increase in heart rate by 30 bpm or more within 10 minutes of standing, often causing dizziness, palpitations, and fatigue
- Polydipsia and dehydration: Excessive thirst, particularly nocturnal, is associated with chronic dehydration and altered thirst regulation. This symptom may be exacerbated by autonomic dysfunction, which impairs fluid balance and increases the risk of electrolyte imbalances. These imbalances contribute to dizziness, fatigue, and muscle cramps, and are common in people with autonomic dysfunction, making fluid and electrolyte management important
- Postural hypotension: A temporary drop in blood pressure upon standing, caused by impaired autonomic regulation of blood volume and vascular tone. This leads to dizziness, lightheadedness, or fainting, especially after standing, and is exacerbated by autonomic dysfunction, which affects the body's ability to regulate blood pressure and circulation. The drop in blood pressure is often accompanied by an increased heart rate as the body compensates for poor circulation and blood pooling in the lower extremities. Visual symptoms such as blackouts, blurriness, grey spots, double vision, and other disturbances can occur due to insufficient blood flow to the brain during these episodes
- Pupil dilation abnormalities: Impaired constriction and dilation responses, including sluggish reactions and enlarged pupils, leading to photophobia, difficulty adjusting to light changes, eye strain, and headaches due to dysregulation of the PNS (parasympathetic nervous system)
- Respiratory dysfunction: Involves impaired respiratory mechanics, leading to dyspnea (shortness of breath), shallow breathing, and fatigue during exertion. Autonomic dysfunction contributes to poor regulation of respiratory patterns, often triggering episodes of shortness of breath during physical activity or at rest, including tachypnea (rapid breathing) that occurs with exertion or stress due to impaired autonomic regulation of respiratory rate. This dysfunction results in shallow or rapid breathing, shortness of breath, and respiratory fatigue
- Restlessness and impaired sleep: Involves restlessness, pacing, or fidgeting, combined with disrupted sleep patterns such as non-restorative sleep, frequent awakenings, and excessive daytime sleepiness. This is often secondary to autonomic instability (dysfunction of the autonomic nervous system), poor circadian regulation (disruption of the body's natural sleep-wake cycle), and inadequate recovery during sleep. Autonomic dysfunction often leads to disturbed sleep patterns, poor sleep quality, and daytime sleepiness due to poor circadian rhythm regulation (the body's internal clock not aligning properly with the natural day-night cycle)
- Sensation of fullness in the chest: Caused by blood pooling, tachycardia, and breathing changes due to autonomic dysregulation

- Sensory overload and sensory distortions: Heightened sensitivity to sensory stimuli (e.g., sound, light, touch, texture) or dysesthetic sensations (e.g., tingling, burning), often due to autonomic dysfunction affecting sensory processing. This includes altered perceptions, such as photophobia (sensitivity to light) and hyperacusis (sensitivity to sound), which may lead to discomfort, difficulty processing sensory input, and increased sensitivity to environmental stimuli. These hypersensitivities can be debilitating in daily life, making it challenging to tolerate routine activities and overwhelming the individual with sensory input
- Severe fever-like symptoms (e.g., extreme coldness, shivering, loss of oxygen to lips, clamminess):

Due to autonomic dysregulation, immune dysfunction (autoimmune or infection-related), and vascular issues (blood flow and vascular tone), leading to temperature dysregulation.

Associated with: Postural Orthostatic Tachycardia Syndrome (POTS), autoimmune dysautonomia, ME/CFS (Myalgic Encephalomyelitis/Chronic Fatigue Syndrome), intracranial hypotension, or adrenal insufficiency which may cause temperature dysregulation, fatigue, and flu-like symptoms due to low cortisol levels

- Sexual dysfunction: This includes dizziness, low libido, inability to orgasm, painful sex, reduced arousal, genital sensitivity issues, fatigue during sex, pelvic discomfort, decreased lubrication, sexual performance anxiety, increased heart rate or palpitations, and worsening symptoms like nausea post-activity. These issues can be attributed to hormone imbalances, altered regulation of blood flow, and stress responses, often exacerbated by autonomic dysfunction or related conditions
- Side stitches (ETAP - Exercise-Related Transient Abdominal Pain): Blood flow irregularities and poor circulation during exercise can lead to cramping in the diaphragm and abdominal muscles, causing worsening discomfort. Poor circulation impacts the muscles' ability to function properly during activity. Additionally, musculoskeletal factors, including joint instability and weakened connective tissue, can contribute. The muscles and ligaments around the diaphragm may experience increased strain or discomfort during physical activity, making it harder to maintain proper posture and increasing the likelihood of side stitches
- Sitting frequently: Aids in preventing blood pooling and helps stabilize circulation when standing
- Sleep and circadian rhythm disruptions: Insomnia, fragmented sleep, excessive daytime sleepiness, and irregular sleep-wake cycles resulting from autonomic dysfunction, including fluctuating heart rate, blood pressure instability, poor circulation, and non-restorative sleep. These disruptions impair circadian regulation, leading to poor-quality sleep, persistent fatigue, and daytime somnolence
- Skin discoloration or rashes: Some individuals may experience changes in skin color, such as redness, paleness, or darkening, or other rashes due to blood flow issues
- Stress-induced symptom exacerbation: An exacerbation of symptoms during physical or emotional stress, resulting from dysregulated stress response mechanisms and increased sensitivity to autonomic stimuli, leading to heightened physiological responses and symptom flares
- Tachycardia when lying down: Some may experience an abnormally high heart rate even while lying down, possibly worsening upon shifting positions
- Temperature asymmetry: Cold hands/feet while the rest of the body is warm or vice versa, due to autonomic dysfunction affecting blood flow

- Thermoregulatory dysfunction: Characterized by temperature sensitivity, heat intolerance, cold extremities, and difficulty maintaining thermal homeostasis in fluctuating environmental conditions. Symptoms may include excessive sweating, cold sweats, hot flashes, impaired thermoregulatory responses, impaired temperature sensation, hot hands/feet, and difficulty maintaining body temperature. This can contribute to extreme discomfort in varying temperatures and is often due to impaired blood flow redistribution to the skin and extremities
- Tinnitus or ear fullness: Feeling of fullness or ringing in the ears, potentially linked to autonomic dysfunction affecting inner ear pressure and blood flow
- Urinary/renal symptoms: May manifest as nocturia, urinary urgency, overactive bladder, or neurogenic bladder, often resulting from autonomic dysregulation of bladder control mechanisms and impaired sensory feedback from the bladder. Bladder dysfunction, including frequent or incomplete emptying, may also occur. Electrolyte imbalances can result from improper fluid regulation, while kidney involvement may arise from altered blood flow or impaired function, contributing to issues with fluid and waste filtration. Both the autonomic nervous system's role and potential structural connective tissue issues can lead to these complications
- Using mobility aids: Provides support for balance and reduces strain on the cardiovascular system, helping to manage dizziness and fatigue
- Vagus nerve dysfunction: Dysfunction of the vagus nerve, leading to impaired regulation of cardiovascular tone, gastrointestinal motility, and inflammatory responses. This contributes to autonomic dysregulation, poor digestion, and irregular heart rate responses
- Vasomotor instability and vasodilation issues: Due to autonomic dysfunction and impaired regulation of blood vessel tone, this common symptom leads to abnormal blood vessel dilation and constriction, causing insufficient blood flow to the brain and other organs, especially when standing. Symptoms include dizziness, lightheadedness, blood pooling, temperature dysregulation, and fainting. These issues are exacerbated by vasodilators such as marijuana, heat, alcohol, and certain medications
- Vertigo, room-spinning sensation, and sensory overload: Episodes of vertigo, dizziness, and spatial disorientation can result from a combination of vestibular dysfunction, autonomic dysregulation, and sensory processing overload. Autonomic dysfunction, particularly impaired regulation of blood flow, can cause dizziness, lightheadedness, or vertigo, especially when standing or changing positions. This is due to insufficient cerebral perfusion, leading to difficulty maintaining balance and spatial awareness
- Visual disturbances: Blurred vision, difficulty focusing, double vision (diplopia), photophobia, visual snow, dry eyes, and "greying out" when standing, often triggered by postural changes, physical exertion, or autonomic fluctuations affecting blood flow to the eyes or brain
- Worsening symptoms with prolonged activity: Exertion intolerance, fatigue, and exacerbation of symptoms such as orthostatic intolerance, cardiovascular instability, and musculoskeletal pain, particularly with prolonged sitting, standing, or walking

Autoimmune System Symptoms:

- Autoimmune POTS: A form of POTS where the immune system attacks the autonomic nervous system, causing blood flow issues and tachycardia upon standing. Symptoms include dizziness, lightheadedness, fatigue, brain fog, blood pooling, cold extremities, nausea, and exercise intolerance

Cardiovascular (CV) System Symptoms:

- Baroreceptor dysfunction and blood pressure variability: Characterized by significant fluctuations in blood pressure, including hypertension, hypotension, and postural hypotension, often exacerbated by orthostatic instability and impaired baroreceptor sensitivity. These fluctuations, which can involve temporary drops in blood pressure (e.g., orthostatic hypotension), are commonly accompanied by dizziness, lightheadedness, or syncope, particularly following prolonged standing or exertion, and are a result of autonomic dysfunction and impaired baroreceptor-mediated regulation
- Blood pooling and compensatory tachycardia: The body compensates for poor venous return by increasing heart rate to maintain blood flow to vital organs, which can cause significant discomfort, palpitations, and chest pain
- Cardiovascular and vascular dysfunction: Abnormal cardiovascular regulation occurs due to sympathetic hyperactivation, leading to arrhythmias (e.g., atrial tachycardia), orthostatic intolerance, and cardiovascular instability. Symptoms such as chest pain, dizziness, palpitations, and postprandial tachycardia or bradycardia are common, often exacerbated by changes in posture or after meals. Increased heart rate variability, reduced cardiac output, and vascular instability contribute to impaired blood flow and heart rate regulation, which can worsen musculoskeletal pain, heighten the risk of syncope or cardiovascular collapse, and result in erratic heart rhythms and potential cardiovascular compromise
- Decreased cardiac output: Due to insufficient blood flow or impaired heart function, often resulting from dysregulated sympathetic and parasympathetic control of the cardiovascular system, this can lead to symptoms such as fatigue, dizziness, and chest discomfort
- Dyspnea (air hunger): Irregular and labored breathing patterns associated with exertion or meals, often caused by compromised cardiovascular stability, impaired respiratory function, and autonomic dysregulation. These factors exacerbate the sensation of breathlessness and fatigue during physical activity
- Electrolyte imbalances: Characterized by abnormal electrolyte homeostasis, often presenting as cravings for salty foods, dehydration, and altered thirst perception. These imbalances are associated with dysregulated fluid and sodium retention mechanisms, contributing to systemic fatigue and circulatory instability
- Exercise intolerance: A marked reduction in the ability to tolerate physical exertion, often due to muscle weakness, circulatory dysregulation, and impaired cardiovascular responses. Individuals may experience fatigue, dyspnea, and increased pain with minimal physical activity, leading to exercise-induced deconditioning
- Exertional chest pain: Results from inadequate myocardial perfusion during physical exertion, exacerbating other symptoms like muscle weakness, fatigue, and autonomic dysregulation, leading to significant discomfort and potential cardiovascular distress
- Hyperdynamic circulation: Characterized by an elevated heart rate and increased stroke volume, leading to an exaggerated cardiovascular response. It is commonly associated with symptoms such as fatigue, dizziness, and palpitations
- Hypotension and renal perfusion: Low blood pressure and impaired kidney perfusion due to dysautonomia, which can compromise kidney function over time
- Hypovolemic symptoms: These occur due to reduced blood volume from fluid loss, blood loss, or impaired fluid regulation. Key manifestations include dizziness, lightheadedness, and syncope, especially upon standing, due to insufficient blood volume for adequate blood pressure and organ perfusion. Other symptoms include fatigue, weakness, pallor, tachycardia, and cold

extremities as the body compensates with vasoconstriction. Dehydration is common, with dry mouth, thirst, dark urine, and low urine output. These symptoms worsen with postural changes, exertion, or prolonged standing, leading to blood pooling in the lower extremities. Severe cases may result in hypovolemic shock, with rapid heart rate, shallow breathing, confusion, and cold, clammy skin

- Neurally-mediated hypotension (NMH): A form of autonomic cardiovascular dysregulation characterized by transient or sustained drops in arterial blood pressure precipitated by upright posture, prolonged standing, or other orthostatic stressors. Pathophysiologically, NMH involves exaggerated cardiovagal and sympathetic reflex responses, abnormal baroreceptor sensitivity, and impaired vasoconstrictive compensation, leading to decreased cerebral perfusion and symptoms of presyncope, syncope, dizziness, or fatigue. In POTS and related dysautonomias, NMH may coexist with tachycardia, altered cardiac output, and secondary autonomic-mediated manifestations including pallor, diaphoresis, or palpitations

- Orthostatic intolerance: Primarily driven by abnormal cardiovascular responses, this condition involves a failure of blood vessels to constrict properly upon standing, leading to reduced venous return and impaired blood flow to the brain. Cardiovascular symptoms include rapid heart rate (tachycardia), blood pressure instability (either sharp drops or sudden spikes), and circulatory issues like venous pooling in the lower extremities. These effects are exacerbated by prolonged standing, sudden postural changes, or physical exertion, causing dizziness, chest discomfort, and in some cases, fainting. Poor blood volume regulation and vasodilation contribute to compromised cardiac output and a reduced ability to maintain normal blood pressure, which heightens the risk of syncope and cardiovascular distress. Blood pooling in the legs further worsens circulation, while reduced cardiac output can lead to symptoms such as fatigue and exercise intolerance

- Poor fluid regulation: Stems from impaired blood volume maintenance, fluid retention, and distribution. Dysfunction in renal control mechanisms impairs the kidneys' ability to retain water and sodium, which exacerbates low blood volume and contributes to dehydration. Reduced sodium and water retention leads to hypovolemia, exacerbating blood pooling and reducing organ perfusion. The body struggles to maintain proper vascular tone and blood flow, often causing blood to pool in the lower extremities. This results in dizziness, lightheadedness, and fatigue during orthostatic stress

- Rapid heart rate: Typically an increase of more than 30 beats per minute upon standing, in the absence of underlying cardiovascular pathology, is a hallmark of autonomic dysfunction

- Vascular and circulatory dysregulation: Characterized by abnormalities in vascular tone and circulation, including cold extremities, temperature sensitivity, impaired blood flow, peripheral venous pooling, and hypovolemia (low blood volume). These symptoms arise from venous insufficiency, impaired circulatory function, and autonomic dysregulation, which reduce venous return to the heart and disrupt the regulation of vascular tone and venous muscle contraction. Circulatory instability is exacerbated by postural changes and exertion, contributing to further vascular fragility

- Vasomotor instability: Fluctuations in vascular tone, which contribute to blood pressure instability, impaired thermoregulation, and dysregulated vascular responses, particularly in response to environmental factors or substances like cannabis

- Venous pooling: Blood tends to accumulate in the legs when standing due to improper vasoconstriction, resulting in cold, discolored, or swollen extremities. This further exacerbates orthostatic intolerance and contributes to fatigue and dizziness

Central and Peripheral Nervous Systems (CNS/PNS) Symptoms:

- Abnormal heart rate (tachycardia/bradycardia): Alterations in heart rate, frequently associated with autonomic dysfunction, which disrupts the cardiovascular system's regulation of heart rate and rhythm. This dysfunction can involve both central nervous system (CNS) and peripheral nervous system (PNS) dysregulation
- Allodynia: Pain induced by stimuli that are normally non-painful, resulting from abnormalities in nociceptive processing within the CNS or PNS, leading to hypersensitivity to touch or other sensory inputs
- Aphasia: Transient or persistent impairment of language production and/or comprehension, potentially arising from central nervous system dysfunction associated with autonomic dysregulation in POTS. Cerebral hypoperfusion, altered cortical perfusion, and dysregulated neurovascular coupling may contribute to deficits in expressive or receptive language, word-finding difficulties, and compromised verbal communication, particularly during orthostatic stress or dysautonomia exacerbations
- Ataxia: Impaired coordination or balance, typically due to deficits in proprioception or disturbances in the CNS or PNS. These disruptions affect motor control and spatial awareness, leading to difficulties with movement coordination
- Bladder dysfunction (neurogenic bladder): Urinary symptoms such as incontinence, urgency, or frequency, commonly due to dysfunction in the autonomic or peripheral nervous systems, which affects the bladder's ability to function properly. This involves both CNS and PNS abnormalities impacting bladder control
- Brain fog (cognitive impairment): Difficulty with concentration, memory, and mental clarity, often attributed to CNS dysfunction and frequently compounded by autonomic dysregulation. This impairs cognitive processing and focus
- Chronic headaches (cervicogenic, tension, etc.): Persistent headache patterns that may result from vascular irregularities, cranial nerve involvement, or central processing dysfunction in the CNS. These headaches can manifest with a variety of symptoms, including tension or cervicogenic features
- Cognitive dysfunction: Impaired memory, attention, and executive function, frequently due to dysfunction in the CNS, with autonomic dysregulation further complicating higher cognitive processes and mental functioning
- Dizziness/presyncope: Episodes of lightheadedness or near-fainting, commonly linked to autonomic dysfunction, impaired blood pressure regulation, or vascular instability, involving both CNS and PNS. These episodes can result from an inability to properly regulate blood flow and blood pressure
- Dysautonomia: Dysfunction of the autonomic nervous system (ANS), leading to irregularities in heart rate, blood pressure, digestion, and other involuntary bodily functions. This often disrupts homeostasis and involves both CNS and PNS abnormalities

- Emotional numbness: A detachment from emotional processing, typically associated with autonomic dysregulation or underlying CNS abnormalities, which affect emotional regulation, response to stimuli, and emotional awareness
- Hand tremors: Involuntary shaking of the hands, often caused by CNS dysfunction (such as in movement disorders) or peripheral neuropathy (PNS), both of which impact motor control and neuromuscular coordination
- Impaired balance: Difficulty maintaining equilibrium, often resulting from proprioceptive dysfunction or disturbances in the CNS or PNS. This affects coordination and spatial awareness, contributing to instability
- Impaired temperature sensation: Altered perception of temperature changes, frequently due to peripheral neuropathy (PNS) or CNS dysfunction. These conditions impact sensory processing, resulting in hypothermia or hyperthermia sensations
- Increased fatigue (central/peripheral fatigue): Profound physical and mental exhaustion, often linked to CNS dysregulation, autonomic dysfunction, or impaired energy production. This can significantly affect daily functioning and recovery
- Increased sensitivity to sound (hyperacusis): Heightened sensitivity to sounds, often due to abnormalities in central auditory processing within the CNS, which leads to discomfort or distress in response to typical environmental noises
- Motor and sensory dysfunction: Manifestations such as weakness, numbness, tingling, or pain in the limbs, typically resulting from peripheral nerve damage (PNS). This affects both motor and sensory functions, impacting mobility and sensation
- Myoclonus: Involuntary muscle jerks or twitches, commonly linked to CNS or PNS dysfunction. This condition affects neuromuscular coordination and motor control, often seen in movement disorders
- Neurogenic bladder dysfunction: Impaired bladder control due to autonomic or peripheral nerve dysfunction (PNS), leading to symptoms like urgency, retention, or incontinence. This dysfunction disrupts normal bladder control mechanisms
- Neuropathy: Peripheral nerve damage (PNS) resulting in symptoms such as pain, tingling, weakness, and numbness, often due to injury or disease affecting sensory or motor nerve fibers
- Paresthesia: Abnormal sensations, such as tingling, "pins and needles," or numbness, frequently linked to peripheral neuropathy (PNS) or CNS involvement in sensory processing. This can indicate nerve dysfunction or injury

Endocrine System Symptoms:

- Adrenal insufficiency: A disorder of cortisol deficiency resulting from inadequate adrenal gland function, which disrupts homeostasis and exacerbates autonomic dysfunction by impairing cardiovascular regulation, blood pressure control, and increasing fatigue, thereby intensifying dysautonomia symptoms

- Hyperthyroidism: A condition characterized by excessive thyroid hormone production, leading to an increased metabolic rate. Symptoms include tachycardia, weight loss, anxiety, tremors, heat intolerance, and irritability. Thyroid dysfunction is known to impact autonomic regulation, potentially exacerbating dysautonomia symptoms by altering heart rate control and vascular tone, thus affecting cardiovascular stability

Gastrointestinal (GI) System Symptoms:

- Abdominal cramping and sharp discomfort: These may result from autonomic dysfunction, which disrupts gastrointestinal motility. This impairment can alter gut transit, leading to symptoms like sharp pain, bloating, and irregular bowel movements
- Abdominal fullness or bloating: Early satiety after meals, due to impaired gastric motility or delayed gastric emptying
- Abdominal pain, stomach aches, discomfort, bloating, and nausea postprandially: Frequently occurs after meals due to GI dysmotility, reflux, or autonomic dysfunction impacting digestion and motility. This can include nausea, bloating, constipation, and diarrhea related to autonomic dysfunction affecting gut motility
- Abnormal thirst sensation and chronic dehydration: A persistent and disproportionate sensation of thirst and dehydration, despite adequate fluid intake, commonly resulting from impaired autonomic regulation of fluid balance. This dysfunction affects the body's ability to properly sense hydration needs, exacerbating dehydration and further impairing fluid absorption and retention
- Acid reflux or gastric reflux: Often exacerbated by dysmotility and impaired autonomic regulation of the gastrointestinal tract, with dysautonomia affecting gastric motility and esophageal function
- Autonomic dysfunction: Impairment in the autonomic nervous system regulation, affecting gastrointestinal motility and function
- Appetite fluctuations, difficulty regulating hunger, and malnutrition: Caused by dysautonomia and GI dysmotility, disrupting normal hunger signals, nutrient absorption, and satiety cues, leading to issues such as excessive hunger or inadequate nutrient intake
- Belching: Often associated with GI dysmotility or dysfunction, leading to excessive air swallowing or delayed gastric emptying
- Bowel habit changes: Includes alterations in bowel movements, including constipation, diarrhea, or alternating patterns, related to dysautonomia and GI dysmotility
- Chronic constipation: Difficulty passing stool or infrequent bowel movements caused by autonomic dysfunction, commonly seen in dysautonomia, due to impaired bowel motility and autonomic control of the gastrointestinal system. This condition can be further compounded by dehydration
- Chronic cough: Occurs due to gastroesophageal reflux or as a secondary response to dysmotility-related airway irritation
- Constipation alternating with diarrhea: A pattern of alternating bowel symptoms, frequently seen with GI dysmotility and autonomic dysfunction affecting gut transit time
- Delayed gastric emptying and other motility issues: Resulting from dysautonomia, these disturbances are caused by impaired autonomic regulation of gastrointestinal motility, leading to delayed digestion and transit times

- Dysautonomia-related gastric hypomotility: Reduced gastric motor function caused by autonomic nervous system dysfunction, leading to slowed gastric emptying, impaired peristalsis, early satiety, nausea, postprandial symptoms, and variable appetite. Frequently overlaps with POTS and hEDS-related autonomic impairment
- Dysphagia (difficulty swallowing): Often caused by esophageal motility dysfunction, potentially exacerbated by vocal cord dysfunction or impaired autonomic regulation of swallowing
- Excessive nocturnal thirst and chronic dehydration: Increased thirst during the night, despite sufficient fluid intake, often resulting from dysregulated fluid balance or dehydration. This may be due to impaired thirst perception and altered nocturnal fluid regulation caused by autonomic dysfunction, leading to persistent dehydration during sleep
- Fluid dysregulation or imbalance: Autonomic dysfunction disrupts the regulation of blood volume, sodium homeostasis, and renal function, leading to dehydration, excessive thirst, and fluid retention. These disturbances impair the body's ability to maintain proper fluid and electrolyte balance, contributing to symptoms such as hypotension, dizziness, and gastrointestinal disturbances
- Food sensitivities, intolerances (e.g., high-fat foods), and malabsorption: Gastrointestinal symptoms such as bloating, nausea, and postprandial discomfort are aggravated by autonomic dysregulation, which impairs motility and gastric emptying. This leads to delayed gastric emptying, dysbiosis, and intestinal inflammation. Mast Cell Activation Syndrome (MCAS) further contributes to these issues, causing malabsorption, nutrient deficiencies, and increased sensitivity to food triggers. High-fat foods can exacerbate these symptoms by slowing gastric emptying and worsening discomfort
- GI dysbiosis: Microbial imbalance in the gut, resulting from dysautonomia disrupting gut flora, leading to digestive disturbances, malabsorption, bloating, gas, and increased postprandial symptoms
- Impaired or excessive burping:
Difficulty or inability to burp, or excessive burping, caused by gastric motility issues or esophageal dysmotility, often linked to autonomic dysfunction. This impairs the release of swallowed air, leading to bloating, discomfort, or a sensation of fullness in the stomach or chest
- Increased symptoms postprandially: Worsening of GI symptoms after eating, often due to delayed gastric emptying or autonomic dysfunction impacting digestion
- Intestinal discomfort: Chronic or intermittent discomfort in the intestines, frequently associated with dysmotility, bloating, or altered gut function
- Intestinal motility issues, such as gastroparesis: These result from impaired autonomic regulation of the gastrointestinal system, leading to delayed gastric emptying, bloating, nausea, and difficulty with digestion, often due to dysfunction of the enteric nervous system and vagal control
- Malnutrition: Often a result of impaired nutrient absorption due to autonomic dysfunction impeding digestion and nutrient absorption, dysregulated GI motility, food intolerances, insufficient nutrient intake, or dysbiosis
- Mast Cell Activation Syndrome (MCAS) symptoms impacting gastrointestinal function: GI symptoms such as bloating, cramping, and nausea, due to mast cell degranulation and release of histamine or other mediators affecting the gastrointestinal tract
- Memory loss associated with gastrointestinal dysfunction: Cognitive dysfunction, such as memory lapses, potentially exacerbated by malnutrition, dehydration, or autonomic dysfunction

- Mild gastric delay: Subclinical or low-grade impairment of gastric emptying that does not meet full diagnostic thresholds for gastroparesis but produces early satiety, bloating, prolonged postprandial fullness, and intolerance to large or high-fat meals. Common in autonomic dysfunction and connective tissue disorders
- Nausea: Exacerbated by postural changes and gastrointestinal dysmotility, nausea is often linked to delayed gastric emptying or reflux. Autonomic dysfunction disrupts the regulation of nausea through the vagus nerve and other autonomic pathways, leading to chronic or intermittent nausea. This nausea is not always related to motility but reflects an impaired autonomic system's regulation of stomach function
- Nausea postprandially: Common after meals, frequently linked to delayed gastric emptying and autonomic control disturbances, dysmotility, reflux, or food intolerances
- Pain or discomfort in the abdomen: Can be due to gastrointestinal dysmotility, inflammation, or dysbiosis, leading to discomfort or pain after eating or during digestion
- Possible gastroenteritis (GE): Inflammation of the stomach and intestines, characterized by symptoms such as diarrhea, nausea, abdominal pain, fever, headache, muscle aches, fatigue, and anorexia, potentially exacerbated by dysautonomia
- Possible iron deficiency anemia: Symptoms include dizziness, lightheadedness, cold extremities, fatigue, tachycardia, and pallor, often associated with GI malabsorption or chronic blood loss
- Postprandial nausea and GI discomfort: After meals, gastrointestinal symptoms like nausea and discomfort are often worsened by autonomic responses such as blood pooling or reduced perfusion to the gut. These disruptions impair blood flow to the digestive system, leading to delayed gastric emptying, bloating, and nausea. This reflects autonomic dysfunction affecting both digestion and fluid distribution, distinct from motility-related issues like those seen in hEDS
- Sensitivity to specific foods contributing to GI symptoms: Certain foods can trigger gastrointestinal distress, leading to symptoms like bloating, nausea, and diarrhea, often due to food intolerances or malabsorption
- Weight changes: Due to impaired nutrient absorption, often influenced by dysautonomia and gut dysbiosis, can result in unexplained weight gain or loss, commonly associated with gastrointestinal dysfunction, dysmotility, and malabsorption
- Water malabsorption: Reduced ability to absorb water in the gastrointestinal tract, leading to dehydration despite adequate fluid intake. This is commonly related to dysmotility or autonomic dysregulation, exacerbating symptoms of fluid imbalance and contributing to dehydration and overall gastrointestinal distress
- Worsened symptoms during flying: Increased autonomic dysregulation, dizziness, tachycardia, and presyncope, triggered by environmental stressors such as low oxygen, dehydration, blood pooling, and stress at high altitudes

Hematological System Symptoms:

- Blood volume dysregulation: A key feature of POTS is impaired blood volume regulation, characterized by abnormal blood pooling in the lower extremities upon standing. This leads to a reduction in venous return to the heart, resulting in a decreased effective circulating blood volume, which compromises tissue perfusion and contributes to symptoms like dizziness, fatigue, and fainting

- Hemoconcentration: In some individuals, a decrease in plasma volume may occur, leading to hemoconcentration. This condition results in an increased concentration of red blood cells, making the blood thicker and more viscous. Hemoconcentration can exacerbate symptoms such as dizziness, fainting, and increased workload on the cardiovascular system, particularly in conditions like dysautonomia
- Microvascular dysfunction: Autonomic dysregulation can impair blood flow in the microcirculation, the network of smaller blood vessels including capillaries, arterioles, and venules. This dysfunction can contribute to abnormal blood flow, leading to issues such as impaired tissue oxygenation, increased risk of blood clot formation, and microvascular changes that disrupt normal circulatory function

Immune System Symptoms:

- CIRS (Chronic Inflammatory Response Syndrome): Immune dysfunction from biotoxin exposure causes systemic inflammation and vascular issues (microcirculation, intracranial hypotension, blood flow, vascular tone); linked to connective tissue disorders and autonomic dysfunction, also seen in ME/CFS, adrenal insufficiency, hyperthyroidism, and autoimmune dysautonomia. Symptoms include temperature dysregulation, heart rate abnormalities, dizziness, blackouts, palpitations, GI issues, and neurological problems like nerve compression (e.g., CTS, skull clicks), cognitive dysfunction, and systemic effects. Endocrine dysfunctions like hyperthyroidism and adrenal insufficiency contribute to tachycardia, temperature regulation issues, and fatigue
- Possible ME/CFS (Myalgic Encephalomyelitis): Chronic fatigue, cognitive impairment, brain fog, autonomic dysfunction (often worsened by POTS or similar conditions), immune dysfunction (with autoimmune and viral triggers), chronic pain, and sensitivity to stimuli

Lymphatic System Symptoms:

- Chronic swelling after activity: Persistent edema in the lower extremities following physical activity or prolonged standing, often resulting from impaired venous return and blood pooling due to autonomic dysfunction, as well as compromised lymphatic drainage, contributing to fluid accumulation in the tissues
- Discomfort in swollen areas: Swelling in affected limbs or regions can cause sensations of discomfort, tightness, or heaviness, which may result from increased interstitial fluid pressure, leading to mechanical strain on surrounding tissues and nerves
- Fluid retention and puffiness: Sensations of fullness, tightness, or puffiness, especially in the hands, ankles, or face, are often observed during episodes of orthostatic intolerance, where impaired autonomic regulation leads to fluid accumulation due to compromised vascular and lymphatic function

- Increased sensitivity to swelling: Areas with poor lymphatic drainage may exhibit heightened sensitivity or tenderness, particularly when vascular tone is weakened due to autonomic dysfunction, leading to reduced blood and lymphatic flow, thereby exacerbating tissue inflammation and discomfort
- Lymphedema in lower extremities: The presence of persistent swelling in the lower limbs due to dysfunction in the lymphatic system, which is unable to efficiently return interstitial fluid to the circulation during orthostatic stress, resulting in the accumulation of fluid in the tissues
- Peripheral swelling (edema): Edema in the legs, feet, or hands, particularly after prolonged standing, arises from inadequate circulation and reduced lymphatic return, often seen in conditions with autonomic dysregulation, leading to fluid retention in the extremities
- Symptoms of inflammation: Generalized fluid buildup and systemic inflammation, often exacerbated by autonomic dysfunction, where dysregulation of the autonomic nervous system contributes to inflammatory responses, tissue edema, and compromised immune function

Musculoskeletal System (MSK) System Symptoms:

- Articular pain or discomfort: Joint pain resulting from instability, mechanical strain, or inflammatory processes, often exacerbated by connective tissue laxity and poor joint support
- Coat hanger pain: Refers to discomfort in the upper back and shoulder girdle, typically due to myofascial trigger points, postural strain, or altered musculoskeletal mechanics, often exacerbated by autonomic dysfunction
- Compensatory muscle patterns: Altered muscle recruitment and movement patterns due to proprioceptive dysfunction or compensatory responses to pain and instability, often contributing to chronic pain and musculoskeletal dysfunction
- Compromised posture: Increased tendency toward poor posture or slumping due to muscle weakness, joint instability, and pain, which may further contribute to musculoskeletal discomfort
- Decreased flexibility: Reduced range of motion, often due to connective tissue laxity, joint instability, or impaired proprioception
- Delayed recovery from injury: Prolonged healing times for musculoskeletal injuries due to poor collagen synthesis and tissue repair, common in connective tissue disorders
- Fibromyalgia-like pain: Widespread musculoskeletal pain with tenderness, often associated with central sensitization, a process in which the nervous system becomes hyper responsive to stimuli
- Joint hypermobility-related pain: Specific pain at hypermobile joints, often related to excessive movement and strain on ligaments and tendons
- Joint instability: Instability in joints, often due to hypermobility or lax connective tissues, resulting in an increased risk of dislocations, sprains, and other musculoskeletal injuries
- Muscle cramps: Involuntary and painful contractions of the muscles, typically caused by electrolyte imbalances, dehydration, or impaired neuromuscular function
- Muscle tightness: Increased muscle tone or stiffness, which may occur due to altered autonomic regulation of muscle function or compensatory responses to musculoskeletal strain or instability

- Muscle weakness: Reduced muscle strength, potentially due to neuromuscular dysfunction, muscle deconditioning, or insufficient joint stability related to connective tissue abnormalities, leading to difficulty with movement and postural control
- Myalgia: Muscle pain or soreness, often resulting from muscle overuse, inflammation, or dysfunction in connective tissues
- Osteopenia/osteoporosis: Reduced bone density due to connective tissue abnormalities, which may increase the risk of fractures or bone pain
- Post-exertional fatigue: A prolonged state of muscle fatigue following physical activity, frequently observed in dysautonomia and related chronic fatigue syndromes, often linked to impaired circulatory and autonomic responses to exertion
- Postural strain: Discomfort and fatigue related to maintaining posture, often exacerbated by autonomic dysregulation and the inability to efficiently regulate blood flow and muscle tone while standing or sitting for prolonged periods
- Soft tissue injury: Increased susceptibility to strains, sprains, and other soft tissue injuries due to impaired proprioception, muscle weakness, and joint instability
- Spinal instability: Potential for spinal misalignment or subluxations, often due to poor joint stability and connective tissue laxity, leading to neck or back pain, nerve impingement, and headaches
- Tendonitis or tendinopathy: Inflammation or degeneration of tendons, potentially due to altered mechanical stress or joint instability, commonly seen with connective tissue laxity

Neurological System Symptoms:

- Anxiety attacks: Episodes of intense fear or apprehension, often triggered by autonomic dysregulation or sensory overload, leading to physiological manifestations such as tachycardia, hyperventilation, and dizziness
- Cardiovascular and blood pressure dysregulation: Includes erratic blood pressure fluctuations, sudden drops in blood pressure (orthostatic and postprandial hypotension), abnormal heart rhythms (tachycardia, bradycardia, palpitations, arrhythmias), orthostatic tachycardia, and postprandial tachycardia, all resulting from autonomic dysfunction affecting vascular tone and heart rate regulation
- Cerebral hypoperfusion: Symptoms related to insufficient blood flow to the brain, which can result in dizziness, confusion, and difficulty concentrating, especially upon standing or after prolonged activity
- Cognitive and emotional dysregulation: Includes cognitive difficulties such as trouble concentrating, memory impairment, brain fog, and mental fatigue. These symptoms are exacerbated by autonomic instability and an imbalance in the body's stress response systems, with sensory overload or environmental triggers intensifying the impact
- Coordination and balance difficulties: Issues with balance and coordination, potentially linked to cerebellar dysfunction or proprioceptive impairments due to autonomic and sensory abnormalities
- Formication and cutaneous paresthesia (sensory/autonomic): Abnormal somatosensory perceptions of insects crawling, biting, or tingling on the skin, arising from dysregulated peripheral and central nervous system signaling associated with autonomic dysfunction in POTS. Impaired autonomic modulation of cutaneous blood flow, heightened peripheral nerve

excitability, and altered central processing of somatosensory input can produce these paresthetic sensations. Clinically, this may be accompanied by itching, burning, hyperesthesia, or transient dysesthesia, contributing to discomfort, sleep disturbance, and impaired quality of life

- Gastrointestinal and fluid dysregulation: Includes gastrointestinal symptoms like nausea, bloating, constipation, diarrhea, and vomiting, alongside excessive thirst (polydipsia), particularly nocturnal polydipsia, due to autonomic dysfunction

- Headache or head pressure: Frequent headaches, exacerbated by autonomic dysfunction, dehydration, or postural changes, and may include visual disturbances like photopsia. Temple headaches are often caused by blood flow and blood pressure changes, especially during postural shifts, leading to throbbing pain, worsened by standing, and improved by lying down. Symptoms include dizziness, lightheadedness, fatigue, tachycardia, and nausea. Tension headaches result from muscle strain in the neck, shoulders, or upper back due to autonomic dysfunction, poor posture, or compensatory strain, with a dull, constant ache, often described as a tight band around the head or temples, aggravated by stress, lack of sleep, or poor posture. Sinus headaches are caused by sinus inflammation or infection, leading to pain or pressure around the forehead, cheeks, and eyes, with nasal congestion, discharge, fever, and facial tenderness. Cluster headaches are of unknown origin, potentially triggered by stress, causing intense, one-sided pain around the eye or temple, lasting 15 minutes to 3 hours, with symptoms like watery eyes, nasal congestion, and sweating, more likely to involve temple pain or vascular headaches due to autonomic dysfunction

- Musculoskeletal weakness and sensory disturbances: Includes generalized muscle weakness, cramps, spasms, and paresthesia (numbness, tingling, burning), typically resulting from autonomic dysfunction, chronic fatigue, or peripheral nerve involvement

- Neurogenic bladder: Dysfunction of the bladder due to nerve involvement, leading to issues with urine retention or frequency

- Neuropathic dystonia (secondary to neuropathy): A manifestation of nerve damage or dysfunction, caused by sensory or motor nerve impairment, leading to abnormal motor responses such as involuntary muscle contractions or postural distortions. This form of dystonia is often seen in conditions like small fiber neuropathy (SFN) and peripheral neuropathy (PN). Symptoms include muscle spasms, twisting, and abnormal postures, triggered by disrupted sensory feedback or motor control

- Postural and activity intolerance: Includes orthostatic intolerance (difficulty standing due to blood pooling), exacerbation of symptoms with prolonged sitting, standing, walking, or exertion, and post-exercise malaise (PEM), along with dizziness or fainting after eating or standing

- Nystagmus: Involuntary eye movements that can occur with autonomic dysfunction, particularly during changes in position or while focusing on visual tasks

- Possible small fiber neuropathy (SFN) and peripheral neuropathy (PN): including symptoms like nerve pain, numbness, tingling, burning sensations, increased sensitivity to pain, touch, and temperature (allodynia/hyperalgesia), cold hands and feet, and occasional shakiness

- Sensory sensitivities and disassociation: Heightened sensitivity to stimuli like light, sound, and touch, leading to discomfort or distress, alongside cognitive dissociation, derealization, and depersonalization caused by stress or autonomic overload

- Sleep paralysis or hypnagogic hallucinations: Sleep-related disturbances that may occur with autonomic dysfunction, often involving the sensation of being unable to move upon waking or falling asleep, or experiencing vivid hallucinations

- Thermoregulatory dysfunction and sensory changes: Impaired temperature regulation with cold intolerance, heat intolerance, excessive or absent sweating (hyperhidrosis or anhidrosis), and altered temperature sensation. Also includes sensory changes such as tingling, numbness, burning, or altered sensations in hands and feet, often linked to peripheral neuropathy or small fiber neuropathy
- Tinnitus: Ringing or buzzing in the ears, which can be related to autonomic dysfunction affecting inner ear structures

Neurovascular System Symptoms:

- Exercise-induced pruritus (autonomic): Localized or generalized skin itch precipitated by physical exertion, resulting from abnormal autonomic and neurovascular responses characteristic of POTS. Dysregulated sympathetic and cholinergic signaling can lead to inappropriate cutaneous vasodilation, altered blood flow distribution, and mast cell or histamine-mediated hypersensitivity, producing pruritus or paresthesia during or following exercise. Clinically, this may be accompanied by flushing, transient warmth, or dysesthesia, reflecting underlying autonomic dysfunction and impaired regulation of microvascular perfusion

Possible Inappropriate Sinus Tachycardia (IST) Symptoms:

- Abnormal sinus node function: leading to an elevated heart rate at rest or with minimal exertion
- Anxiety: often triggered by rapid heart rates, which can exacerbate symptoms and contribute to a cycle of heightened adrenergic response
- Chest discomfort: mild to moderate, sometimes described as tightness or pressure, which may occur with tachycardia
- Difficulty concentrating or brain fog: potentially due to decreased blood flow or oxygen delivery to the brain during episodes of tachycardia
- Disproportionate tachycardia: in response to minimal activity
- Dysregulation of the autonomic nervous system: resulting in an imbalance between sympathetic and parasympathetic modulation of heart rate
- Elevated blood pressure: which may accompany tachycardia
- Exercise intolerance: due to the inability of the heart to properly increase and manage heart rate during physical activity
- Fatigue: occurring without orthostatic stress
- Lightheadedness or dizziness: occurring with standing or exertion due to inadequate blood flow
- Palpitations: occurring with minimal physical activity or at rest
- Resting tachycardia: with a heart rate typically decreasing upon assuming a supine position
- Shortness of breath: often with minimal physical activity, due to the heart working inefficiently at a high rate
- Sleep disturbances: because of elevated heart rate and anxiety symptoms interfering with rest

Psychological Symptoms:

- Acute feelings of impending doom or panic: A psychological symptom characterized by intense, irrational feelings of fear or dread, often associated with panic attacks and generalized anxiety. These feelings are typically triggered by stress or excitement, and can be exacerbated by autonomic dysfunction, hypotension, or fluctuations in blood pressure and heart rate. These factors heighten sensitivity to stressors, amplifying the sensation through physiological changes, such as altered heart rate, blood pressure, and adrenal stress responses, which can lead to intense feelings of dread or fear without a clear external cause
- Chronic stress and anxiety: Heightened by constant fluctuations in autonomic function, physical discomfort, and the ongoing uncertainty of managing a long-term condition. This results in sustained stress, impacting mood, coping strategies, and mental health
- Fatigue-related mood swings: Extreme fatigue and disrupted sleep can lead to emotional instability, with anxiety, irritability, and mood swings due to the toll on both mental and physical health. Mood swings may occur without clear external triggers, swinging from high anxiety to deep despair
- Health anxiety: Concerns regarding the unpredictability of symptoms, exacerbations, and the long-term trajectory of the condition, compounded by ongoing medical uncertainty

Renal/Kidney and Urogenital System Symptoms:

- Dehydration: Inadequate fluid intake or impaired fluid retention secondary to autonomic dysfunction results in reduced effective circulating blood volume and diminished renal perfusion pressure. The consequent renal hypoperfusion increases physiologic stress on the kidneys, potentially accelerating ischemic injury, impairing glomerular filtration, and contributing over time to the progression of chronic kidney dysfunction
- Hypotension and renal perfusion: Chronic hypotension and compromised renal perfusion resulting from autonomic dysregulation, where impaired control of blood pressure and vascular tone reduces renal blood flow. This can lead to kidney dysfunction and long-term renal complications, including impaired filtration and waste elimination
- Kidney dysfunction: Kidney dysfunction: A condition arising from altered renal blood flow and impaired pressure regulation, resulting in disrupted intraglomerular hemodynamics and compromised autoregulatory capacity. These disturbances lead to abnormalities in glomerular filtration and tubular function, producing clinically significant electrolyte and acid–base imbalances, diminished clearance of metabolic waste products, and—if the underlying hemodynamic impairment persists—progressive renal insufficiency with potential advancement to chronic kidney disease
- Kidney stone formation: Kidney stone formation: An increased predisposition to nephrolithiasis arising from dysregulated renal fluid handling and altered urinary composition. Perturbations in fluid balance and urinary concentration, along with shifts in key lithogenic solutes such as calcium, oxalate, and phosphate, impair normal crystallization-inhibitory mechanisms. Dysautonomia and disrupted renal regulatory pathways can further exacerbate these

physicochemical alterations, collectively enhancing supersaturation and promoting renal stone formation

- Neurogenic bladder: Dysfunction of the bladder due to autonomic or somatic nerve involvement, resulting in impaired bladder filling and emptying. This can lead to urinary retention, urgency, frequency, and incontinence, often observed in individuals with connective tissue disorders and dysautonomia
- Nocturia (frequent urination): Increased nocturnal urinary frequency resulting from autonomic dysregulation and impaired renal mechanisms governing fluid balance. Disruption of normal diurnal fluid and electrolyte handling can lead to excessive nocturnal diuresis or aberrant fluid redistribution, contributing to sleep interruption, altered circadian urine output patterns, and further destabilization of overall fluid homeostasis
- Orthostatic hypoperfusion of the kidneys: A hemodynamic disturbance characterized by reduced renal perfusion upon standing due to autonomic dysfunction and impaired systemic blood flow regulation. The resultant decline in renal blood supply compromises intraglomerular pressure and glomerular filtration efficiency, predisposing to transient or sustained alterations in tubular handling of electrolytes, potential electrolyte imbalances, and increased renal physiologic stress—particularly in individuals with underlying dysautonomia
- Postural fluid imbalance: A disruption of fluid homeostasis occurring during positional transitions—such as moving from supine to upright—driven by autonomic dysfunction and impaired cardiovascular–renal coordination. These abnormalities compromise renal regulation of intravascular volume and sodium–water balance, leading to maladaptive shifts in fluid distribution that may manifest as orthostatic hypotension, ineffective plasma volume expansion, dehydration, or inappropriate fluid retention
- Salt wasting: Excessive renal sodium loss resulting from impaired autonomic regulation of renal hemodynamics and tubular sodium reabsorption. This dysregulation promotes inappropriate natriuresis and predisposes to hyponatremia, extracellular fluid depletion, and secondary disturbances in overall fluid and electrolyte homeostasis. Consequent volume contraction, dehydration, and related physiologic complications may arise when these sodium-handling abnormalities persist
- Urogenital manifestations: Result from autonomic dysfunction and impaired blood flow regulation, leading to urinary frequency and urgency (exacerbated by blood pooling in the lower extremities), nocturia (waking at night to urinate due to fluid balance and blood pressure regulation issues), incontinence (stress or urgency incontinence due to autonomic dysregulation), sexual dysfunction (e.g., reduced libido or difficulty achieving orgasm from blood flow or autonomic issues in the genital region), and chronic pelvic pain (linked to poor blood flow, muscle tension, and autonomic dysfunction in the pelvic region)

Vascular (VS) System Symptoms:

- Hypervascularity: Increased blood flow to peripheral areas (arms, legs, hands, feet), which may cause skin flushing, redness, or a feeling of warmth, sometimes linked to the compensatory mechanisms in autonomic dysfunction
- Impaired thermoregulation: Dysfunction in the autonomic nervous system (ANS), particularly in the regulation of vasodilation and vasoconstriction, disrupts the body's ability to maintain normal thermal homeostasis. This may manifest as intolerance to heat, excessive sweating, or difficulty maintaining body temperature due to impaired blood flow redistribution to the skin and

extremities, often due to exaggerated sympathetic nervous system activity or insufficiency of compensatory vasodilation

- Peripheral edema: Swelling of the lower extremities, typically the legs and feet, resulting from fluid retention. This occurs due to impaired venous return and capillary leak, where increased hydrostatic pressure in the peripheral veins leads to the extravasation of fluid into the interstitial space. This process is compounded by venous insufficiency and autonomic dysfunction that impair vascular tone regulation and lymphatic drainage

- Peripheral venous pooling: Blood accumulation in the lower extremities, often due to venous insufficiency, impaired circulatory function, or autonomic dysregulation, leading to reduced venous return to the heart. This pooling is exacerbated by the inability of the autonomic nervous system to regulate vascular tone and venous muscle contraction effectively, impairing the movement of blood back to the upper body

- Possible may-thurner syndrome: A condition where the right iliac artery compresses the left iliac vein. Symptoms include swelling, pain, and possibly the development of blood clots in the legs

- Postural orthostatic tachycardia syndrome (POTS)-related vascular dysfunction: Beyond pooling and edema, poor vascular tone regulation can lead to inadequate vasoconstriction or dilation during posture changes, potentially resulting in episodes of fainting, dizziness, or blood pressure fluctuations

- Raynaud's phenomenon: Excessive vasoconstriction in response to cold or stress, often due to heightened sympathetic tone, leading to reduced blood flow to peripheral tissues (e.g., fingers and toes). This phenomenon is thought to be linked to sympathetic overactivity and the impaired regulation of vasodilation, resulting in episodes of pallor, coldness, numbness, and sometimes pain in the affected areas due to restricted blood flow

- Vascular dilation: In some cases, there may be excessive blood vessel dilation in response to autonomic dysregulation, leading to symptoms like flushing, headache, and a sensation of warmth or heat intolerance due to ineffective vasoconstriction

Vestibular/ENT System Symptoms:

- Nasal pressure-induced presyncope and barotrauma: Transient presyncopal symptoms and vestibular or auditory disturbances precipitated by forceful Valsalva maneuvers, such as attempting to forcibly exhale through the nares or occluding the nose. In patients with dysautonomia (e.g., POTS), impaired autonomic cardiovascular regulation reduces cerebral perfusion during increased intrathoracic and intranasal pressures, while altered eustachian tube function and vestibular sensitivity contribute to tympanic membrane stress, aural fullness, and dizziness

- Transient hearing loss preceding syncope (vestibular/ENT-autonomic): Episodic reduction or loss of auditory perception and/or vestibular symptoms (aural fullness, ear-popping, tinnitus, dizziness) occurring immediately before or during pre-syncope or syncope. This may result from autonomic-mediated cerebral hypoperfusion or dysregulated inner-ear blood flow, compounded by impaired baroreflex and vascular autoregulation typical of POTS. The consequent decreased perfusion pressure in cochlear or vestibular vascular beds, combined with rapid shifts in intrathoracic and vascular pressure, can transiently compromise cochlear and vestibular function — producing hearing attenuation or vestibular symptoms, potentially serving as a “prodrome” to syncope

Shared hEDS and POTS Symptoms

- Altered sweating response: Resulting from autonomic dysfunction, which disrupts the regulation of thermoregulatory and sudomotor pathways. This leads to episodes of abnormal sweating, including hyperhidrosis or anhidrosis, occurring without typical triggers such as exercise or heat
- Anxiety: Heightened anxiety arising from symptom management, fear of exacerbations, and uncertainty about the future
- Chronic fatigue: A persistent feeling of extreme tiredness not relieved by rest, often exacerbated by orthostatic intolerance, musculoskeletal instability, and poor circulation
- Chronic pain: Due to musculoskeletal strain and poor circulation, chronic pain is a common symptom of dysautonomia
- Cognitive difficulties, including impaired memory, concentration, and mental clarity (often referred to as brain fog): These impairments are exacerbated by fatigue, autonomic dysfunction, and neurocognitive disruption, with reduced cerebral perfusion and blood pressure instability potentially contributing. As a result, individuals may withdraw from social activities or relationships, leading to social isolation and further amplifying the emotional burden
- Compulsive behaviors or tendencies, including obsessive thoughts or actions (OCD-like tendencies): These may arise due to autonomic nervous system dysregulation, which can cause heightened states of stress or anxiety that manifest in compulsive behaviors
- Crepitus (joint cracking or popping): Due to hypermobility and ligament laxity, joints may move beyond their normal range, causing cracks or pops. This can lead to discomfort or instability, particularly during weight-bearing activities. Autonomic dysfunction may worsen these symptoms by affecting muscle tone and proprioception, making joint movements more pronounced or painful
- Delayed response to stress: The body's reaction to stress is not immediate but instead is prolonged or delayed. Individuals may experience a lag in physical or emotional responses, leading to delayed symptoms such as fatigue, anxiety, or physical discomfort. This occurs due to disruptions in the autonomic nervous system, which impair the body's ability to process and manage stress in real time. As a result, recovery from stress takes longer, leaving individuals feeling overwhelmed or drained after the event
- Depressive symptoms, including low mood and feelings of hopelessness: Emotional symptoms are common, likely due to chronic pain, physical limitations, and neurochemical imbalances caused by autonomic dysfunction, with persistent pain, fatigue, and functional impairments contributing to sadness, loss of interest in daily activities, and reduced motivation
- Derealization experiences, characterized by a sense of detachment from reality or altered perception of the environment: This may be linked to neurological disturbances related to orthostatic changes in blood flow, or a direct impact of autonomic dysfunction on brain function and sensory integration issues
- Difficulty maintaining upright posture, with a tendency to require frequent sitting or leaning for support: The result of orthostatic intolerance and musculoskeletal instability, both of which contribute to a decreased ability to maintain upright postural control due to hypotension and joint laxity

- Difficulty regulating heart rate and blood pressure: Dysautonomia can cause variability in heart rate and blood pressure, with rapid changes when transitioning between sitting, standing, or lying down
- Difficulty sustaining focus and concentration over extended periods: Typically due to cognitive dysfunction from hypoperfusion and musculoskeletal discomfort or pain, both of which interfere with concentration and mental clarity
- Dysphagia (difficulty swallowing): Autonomic dysfunction can exacerbate difficulty swallowing by affecting the coordination of muscles required for the process
- Emotional dysregulation, including heightened sensitivity to anxiety, panic, and mood swings: The autonomic instability can increase sensitivity to emotional stress, and collagen abnormalities can affect neurotransmitter function, both contributing to mood instability. This can lead to emotional numbness as a coping mechanism
- Excessive daytime somnolence or frequent yawning: A direct manifestation of autonomic dysfunction, where improper regulation of sleep-wake cycles and poor blood circulation contribute to persistent fatigue
- Eye discomfort: Due to connective tissue issues, this can lead to dryness, irritation, or strain on eye muscles. It can also be caused by poor blood flow, with autonomic dysfunction contributing to dryness, light sensitivity, and visual discomfort
- Frequent changes in body temperature:
A key symptom of dysautonomia, often characterized by hypersensitivity to cold temperatures (cold intolerance). This occurs when the ANS (autonomic nervous system) fails to properly regulate body temperature. The inability to maintain stable temperatures is exacerbated by poor circulation, hypotension, and collagen-related connective tissue abnormalities that interfere with the body's normal thermoregulation processes
- Frequent need to adjust clothing: Especially when experiencing physical discomfort or changes in body temperature, this can be tied to temperature regulation issues, where poor thermoregulation and musculoskeletal discomfort prompt frequent adjustments
- Frequent use of disclaimers like "I'm fine," to mask symptoms: This can be a coping mechanism due to the invisibility of symptoms or social stigma associated with chronic conditions, leading individuals to hide their struggles
- Frequent urination at night and overactive bladder: Caused by autonomic dysfunction, which disrupts normal bladder control and fluid regulation. This leads to symptoms such as nocturia and an overactive bladder, characterized by frequent, urgent urination even with minimal fluid intake. Autonomic dysregulation impairs the bladder's ability to properly store and void urine, resulting in these urinary symptoms
- Frustration and helplessness: The unpredictability of symptoms creates feelings of frustration and helplessness, particularly when symptoms prevent normal functioning and the search for effective solutions remains elusive
- Gastrointestinal dysregulation, including symptoms like bloating, constipation, or nausea: Affected gut motility and intestinal hypermobility, leading to gastrointestinal issues due to autonomic dysfunction
- Generalized body aches: Widespread muscle and joint pain caused by joint instability, connective tissue weakness, and impaired circulation. Autonomic dysfunction and muscle fatigue further exacerbate the pain by disrupting blood flow regulation

- Heat and cold intolerance, with difficulty regulating body temperature in warm and cold conditions: A result of autonomic dysregulation, where the body's ability to sweat and cool down is impaired, exacerbated by hypotension and blood flow and circulation issues
- Hormonal changes affecting mood: Caused by autonomic dysfunction disrupting the regulation of mood-related hormones (e.g., cortisol, serotonin), leading to mood swings, anxiety, or depression due to hormonal imbalances
- Impaired memory function, including frequent forgetfulness: Associated with both dysautonomia and cognitive dysfunction related to hypoperfusion of the brain, compounded by joint and nerve compression issues
- Increased frequency of unintentional collisions or spatial disorientation, particularly during distraction or fatigue: A result of proprioception impairment, joint instability, or sensory processing issues, compounded by dysautonomia and orthostatic intolerance
- Increased frequency of unintentional object drops: Linked to neurological deficits, such as sensory or proprioceptive disturbances, combined with dysautonomia and muscle weakness that reduce coordination and dexterity
- Increased susceptibility to colds: Resulting from autonomic dysfunction, which impairs immune system regulation and reduces the body's ability to mount an effective defense against infections. This leads to a heightened vulnerability to viral illnesses, such as the common cold
- Intermittent low-grade fever without clear etiology: Possibly linked to autonomic dysfunction, inflammatory processes, or mast cell activation syndrome (MCAS), which can be present in both conditions and cause cytokine release or low-grade fever
- Joint discomfort or misalignment: The laxity of ligaments can lead to joint misalignment, contributing to pain and discomfort, especially when combined with autonomic dysfunction, which can interfere with coordination and muscle function
- Joint instability and subluxations: Weakened connective tissue and impaired blood flow may lead to joint instability, which can cause painful subluxations and discomfort
- Muscle twitches: Caused by autonomic dysfunction and muscle fatigue, resulting from poor circulation, abnormal nerve signaling, or prolonged tension. These involuntary contractions, often in the limbs, can be worsened by stress, fatigue, or postural changes
- Need to manage symptoms covertly, often to avoid drawing attention: Due to the invisible nature of many symptoms, individuals may feel the need to hide their symptoms to avoid stigma or misunderstanding
- Neurogenic pain: Pain caused by nerve dysfunction, which can include burning, tingling, or shooting sensations. This may result from small fiber neuropathy or other neurological disturbances linked to dysautonomia
- Orthostatic intolerance: A hallmark of dysautonomia, it involves difficulty standing or maintaining an upright posture for long periods due to inadequate blood flow and autonomic regulation, often causing dizziness or fainting
- Persistent physical restlessness, such as fidgeting or frequent positional adjustments: This is often tied to autonomic dysregulation, pain, or musculoskeletal discomfort from joint instability and weakness, as well as an attempt to manage blood pressure or improve circulation
- Persistent thirst: This occurs when disruptions in fluid balance regulation lead to a constant feeling of thirst, even when hydration levels are adequate. It can result from impaired blood flow, autonomic dysfunction, or electrolyte imbalances, affecting the body's thirst signals and fluid management

- Premature departure from events or activities: Often driven by fatigue, autonomic instability, or discomfort related to joint instability or postural challenges. This may occur due to both dysautonomia and hypermobility-related pain
- Recurrent cancellation of plans due to unpredictable symptom fluctuations: A result of variable symptom presentation where autonomic instability and pain episodes can lead to unpredictable changes in energy levels and mobility
- Restlessness: A symptom characterized by a persistent urge to move or an inability to relax, often manifesting as physical fidgeting or mental agitation. This can result from autonomic nervous system dysfunction, impairing regulation of energy, rest cycles, and sensory processing, leading to ongoing discomfort and difficulty focusing
- Sleep disturbances: Common issues like insomnia, frequent awakenings, non-restorative sleep, and daytime fatigue caused by autonomic dysregulation, discomfort, or circadian rhythm disturbances. Chronic pain, joint instability, and discomfort from musculoskeletal manifestations contribute to difficulty falling or staying asleep, leading to disrupted rest, cognitive dysfunction, and emotional instability
- Sleepiness after meals: Postprandial somnolence occurs when blood flow is redirected to the digestive system, reducing circulation elsewhere and causing temporary fatigue. Autonomic dysregulation may impair glucose and metabolic control, further contributing to drowsiness. This results in increased fatigue or lethargy after meals, even with minimal food intake
- Spontaneous bruising: A symptom where bruises appear without noticeable trauma, often due to increased vessel fragility. This can result from structural defects in blood vessel walls, such as weakened collagen or elastin, leading to capillary rupture and blood leakage into surrounding tissues. Minor pressure or everyday activity can cause these spontaneous hematomas
- Tinnitus: Ringing or buzzing in the ears, which can be linked to autonomic dysfunction, especially when combined with vascular issues
- Variability in symptoms based on activity level: Due to autonomic dysregulation, where impaired control of cardiovascular, metabolic, and vascular responses causes symptoms to fluctuate with physical exertion. Increased activity can exacerbate symptoms, while rest may temporarily alleviate them, reflecting disrupted homeostatic mechanisms
- Weakness in arms or legs: Caused by impaired neuromuscular function, autonomic dysregulation, and reduced blood flow, leading to muscle fatigue, decreased strength, and difficulty with movement or posture, particularly in the limbs
- Weight gain or loss: Resulting from autonomic dysregulation affecting metabolism, appetite regulation, malabsorption, and increased energy expenditure, leading to either excessive weight gain or unintended weight loss

Other

Genetic:

- 7q11.23 (Genetic Region): A genetic and neurodevelopmental region associated with conditions like Autism Spectrum Disorder (ASD) and others, often presenting neurological features, including sensory processing disorders (SPD) and related sensory processing issues

Neurological Symptoms:

- Mild Hypotonic Cerebral Palsy: A neurological condition characterized by reduced muscle tone and impaired motor control, leading to muscle weakness, coordination difficulties, and musculoskeletal challenges
- Narcolepsy: A neurological disorder affecting sleep regulation, often accompanied by autonomic features due to dysregulation in sleep/wake cycles, and frequently seen alongside autonomic issues in related conditions