Nursing Management of Patients with Ehlers–Danlos Syndrome

A guide to this underrecognized, often debilitating condition.

OVERVIEW: Ehlers–Danlos syndrome (EDS), a hereditary connective tissue disorder, has historically been misunderstood and underdiagnosed by health care providers. Because of the high degree of phenotypic variability, patients are often correctly diagnosed only after years of seemingly unrelated but debilitating injuries and illnesses. Specific genetic mutations have been identified for some, but not all, EDS types; patients presenting with a high index of suspicion should be referred to a geneticist. As awareness and recognition of the syndrome improve, nurses are increasingly likely to care for patients with EDS. This article gives a brief overview of the syndrome and provides guidance on ways to manage symptoms, recognize and prevent serious complications, and improve patients' quality of life.

Keywords: collagen, connective tissue, Ehlers–Danlos syndrome, genetic illness, pain, quality of life

Ehlers–Danlos syndrome (EDS) refers to a group of hereditary connective tissue disorders which together affect an estimated one in 5,000 persons worldwide.[1] The condition is likely underdiagnosed because of a lack of familiarity with its various manifestations and a lack of consensus regarding diagnostic criteria.[2, 3]

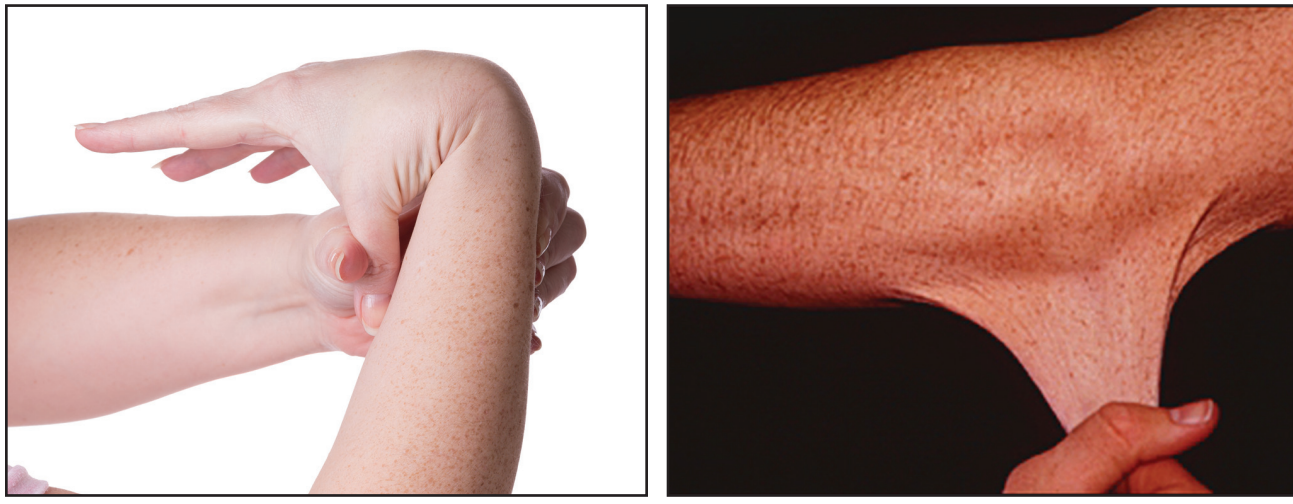
There is little mention in the nursing literature regarding EDS. Nurses are generally unfamiliar with the condition's signs and symptoms, and few health care organizations have established clinical protocols for assessing and managing these patients. Recently, as the medical literature regarding EDS has grown, the health care community's awareness of this condition has expanded, and patients with EDS are educating themselves in order to manage their health. It's imperative that nurses familiarize themselves with the often disabling, sometimes life-threatening clinical manifestations of this syndrome.

BACKGROUND AND CLASSIFICATION

The primary symptoms of EDS include skin extensibility, joint hypermobility, and general tissue fragility.[4] The syndrome was first comprehensively described in the late 19th century as a condition with lax, fragile skin and loose joints; Parapia and Jackson have noted that some people with the condition "displayed their hyperextensibility as performers at travelling shows" and circuses of the era.[5] During the early 20th century the syndrome gained further attention following case reports by Danish dermatologist Edvard Ehlers and French dermatologist Henri-Alexandre Danlos, for whom the syndrome was later named.

Early classification systems described more than 10 types of EDS.[1] In 1997, Beighton and colleagues created a simpler system, defining major and minor diagnostic criteria for six basic types of EDS, and this system remains in use today (see Table 1[4]).[4]

The presence of one or more major criteria is highly indicative of EDS; the presence of minor criteria may suggest an EDS-like condition, but is insufficient for diagnosis in the absence of major criteria.[4] The most common types of EDS are the classical type (formerly known as EDS I and EDS II) and the hypermobility type (EDS-HT); together these account for approximately 90% of all diagnosed cases.[6] The



Joint hypermobility and skin hyperextensibility are examples of the most common types of Ehlers–Danlos syndrome. Photos (left to right) © Suzbah / Dreamstime.com and © A.D.A.M., Inc. 2015.

incidence of the vascular type (VEDS; formerly known as EDS IV), the most serious form of EDS, has been estimated at one in 250,000 people.[6] The remaining three types of EDS (kyphoscoliosis type, arthrochalasia type, and dermatosparaxis type) are extremely rare.[6]

PATHOPHYSIOLOGY

Collagen, a major protein component of connective tissue, functions to increase tissue elasticity and resistance to deformation. Hereditable disorders of connective tissues, such as EDS, can arise as a result of genetic mutations that either alter the structure of collagen or cause deficiencies in enzymes involved in its synthesis.[2,7] Abnormal collagen leads to reduced elasticity of connective tissue. Since connective tissue provides structural support for organs throughout the body, alterations can result in a range of systemic and variable defects of the joints, skin, vessels, and organs.[7]

DIAGNOSIS

Specific genetic mutations have been identified for some, but not all, EDS types.[4] Particular mutations affect specific types of collagen, which then determine the clinical manifestation of the syndrome. Because of the high degree of phenotypic variability, patients may be correctly diagnosed only after years of seemingly unrelated but debilitating injuries and illnesses. General medical practitioners may be ill equipped to provide the genetic evaluation and testing required for a definitive diagnosis; patients presenting with a high index of suspicion should be referred to a geneticist. Genetic evaluation for EDS involves a thorough physical examination that includes determining a Beighton score for hypermobility (see Table 2[8]), scrutinizing the skin for any wounds or scars, and taking medical and family histories.[7] In some cases blood or tissue tests (or both) may be performed to determine EDS type and to rule out other connective tissue disorders that present similarly.[7]

In autosomal dominant syndromes, inheriting the associated genetic mutation from just one parent is sufficient for the syndrome's manifestation; in turn, each child of an affected individual has a 50% chance of inheriting the mutation. While most types of EDS appear to be autosomal dominant, two of the rarer types (kyphoscoliosis and dermatosparaxis) are autosomal recessive[4]; that is, inheriting the genetic mutation from both parents is necessary for the syndrome's manifestation.

But with most types of EDS, the genetic inheritance doesn't necessarily correlate with the eventual clinical outcome. For example, with classical EDS, no distinct genotype–phenotype correlations have been defined.[9] Moreover, family members can share an EDS genotype but manifest the syndrome differently. Genetically, it may be difficult to distinguish autosomal dominant inheritance from spontaneous (de novo) mutation, as symptom variability among family members may lead to an overall failure to recognize the condition.[10] This variability, as well as some overlap in signs and symptoms across EDS types, can complicate differential diagnosis.

The specific genetic mutation underlying EDS-HT, the most common type, is unknown in most cases.[6] Diagnosis is based on family history and

Table 1. Ehlers–Danlos Syndrome: Revised 1997 Nosology[4]

Type	Major Criteria	Minor Criteria
Classical	• Skin hyperextensibility • Widened atrophic scars (sign of tissue fragility) • Joint hypermobility	• Smooth velvety skin • Molluscoid pseudotumors • Subcutaneous spheroids • Complications of joint hypermobility (such as sprains, dislocations, subluxations) • Muscle hypotonia; delayed gross motor development • Easy bruising • Signs of tissue extensibility and fragility (such as hiatal hernia) • Surgical complications (such as postoperative hernia) • Positive family history
Hypermobility	• Skin involvement (hyperextensibility, smooth velvety skin, or both) • Generalized joint hypermobility	• Recurring joint dislocations • Chronic joint or limb pain • Positive family history
Vascular	• Thin, translucent skin • Arterial, intestinal, or uterine fragility or rupture • Extensive bruising • Characteristic facial appearance	• Acrogeria • Small-joint hypermobility • Tendon and muscle rupture • Talipes equinovarus (clubfoot) • Early-onset varicose veins • Arteriovenous, carotid–cavernous sinus fistula • Pneumothorax or pneumohemothorax • Gingival recession • Positive family history; sudden death of one or more close relatives
Kyphoscoliosis	• Generalized joint laxity • Severe muscle hypotonia at birth • Scoliosis at birth, progressive • Scleral fragility and ocular globe rupture	• Tissue fragility, including atrophic scars • Easy bruising • Arterial rupture • Marfanoid habitus • Microcornea • Radiologically considerable osteopenia • Positive family history
Arthrochalasia	• Severe generalized joint hypermobility with recurrent subluxations • Congenital bilateral hip dislocation	• Skin hyperextensibility • Tissue fragility, including atrophic scars • Easy bruising • Muscle hypotonia • Kyphoscoliosis • Radiologically mild osteopenia
Dermatosparaxis	• Severe skin fragility • Sagging, redundant skin	• Soft, doughy skin texture • Easy bruising • Premature rupture of fetal membranes • Large hernias (umbilical, inguinal)

clinical criteria, including current or past joint hypermobility, joint subluxations or dislocations (or both), and chronic limb pain.[6] Inheritance is autosomal dominant, but in a small number of cases it's autosomal recessive.[6] It's also not known why EDS-HT is more common among women than men.[6, 11, 12] One possible explanation is that some people inherit an asymptomatic form of the syndrome, and that extrinsic factors such as body weight, diet, sports and other physical activities, and trauma then play a role in how it manifests.[2]

Although this article focuses primarily on adults with EDS, children can also be diagnosed with the syndrome. There is little in the medical literature regarding EDS in pediatric patients. Evaluation of skin extensibility can be complicated by the abundance of

subcutaneous fat in children.[9] Asymptomatic joint hypermobility is common in young children, making diagnosis (particularly of EDS-HT) more difficult.[2, 10] Children older than 10 years of age should be examined and followed clinically if a definitive diagnosis of EDS-HT has been made in a first-degree relative (such as a parent or sibling).[10] Children with VEDS may be diagnosed early following a vascular complication; about 25% of VEDS patients experience "a significant medical problem" before the age of 20.[9]

Logistical considerations may also impede definitive diagnosis of EDS. First, only a few clinical centers nationwide have clinicians who are familiar with EDS assessment and resources for testing. A patient's access to such clinical evaluation may be limited by distance or by financial constraints. Some patients have reported that their physicians resist referring them to a geneticist, presumably because of a lack of understanding of the clinical advantages of early diagnosis.[13, 14] Some patients may fear receiving a clinical diagnosis of a chronic condition, because of fears about potential discrimination by employers and social contacts.[15] Still, as with other complex heritable conditions, an accurate diagnosis is essential to patient care in order to ensure proper monitoring of symptoms and for potential complications, help patients adjust their expectations and lifestyles to accommodate the condition, and foster the identification of other at-risk family members.

CLINICAL MANIFESTATIONS

It's difficult to quantify the prevalence of various clinical manifestations in EDS patients, and this continues to complicate the process of characterizing the syndrome. Since EDS is usually diagnosed late, well after patients first seek treatment for a variety of maladies, it's likely that the pool of study subjects has disproportionately included patients who are more symptomatic. It's not known what proportion of EDS patients are as yet undiagnosed because they have few or no symptoms, or what proportion will eventually face significant impairment. That said, of the patients who have been diagnosed and studied, the following clinical manifestations are commonly encountered.

Dermatologic. Skin hyperextensibility, a primary feature of EDS, is most pronounced in the classical type.[2, 9] Testing should be done in a neutral area ("one not subjected to mechanical forces or scarring"); the degree of extensibility is measured by pulling up the skin until resistance is felt.[9] An adult's skin is considered hyperextensible if it can be stretched 1.5 cm or more at the dorsum of the hand or the volar aspect of the forearm.[2] The skin and underlying tissues also tend to be fragile, as indicated by skin splitting upon relatively minor trauma, widened atrophic scars, prolonged wound healing, and easy bruising.[9] Extensive bruising, particularly in the presence of thin, translucent skin, may be indicative of VEDS.[4] In cases of significant bruising, particularly in children and other vulnerable populations, careful evaluation to rule out abuse or other nonaccidental trauma is essential.

Table 2. Beighton Hypermobility Scale[8, a]

Assess for the ability to perform each of the following:	Right	Left
1. Passive dorsiflexion of the little fingers beyond 90°	1	1
2. Passive apposition of the thumbs to the flexor aspects of the forearms	1	1
3. Hyperextension of the elbows beyond 10°	1	1
4. Hyperextension of the knees beyond 10°	1	1
5. Forward flexion of the trunk, with knees straight, so that the palms of the hands rest easily on the floor	1	
Total	9	

[a] Scoring: One point is allocated for each positive answer. The total possible score ranges from 0 to 9.

Musculoskeletal. Joint hypermobility refers to the ability of joints to move beyond their normal range, and can be assessed using the Beighton hypermobility scale.[8] In itself, joint hypermobility is a common clinical observation, particularly in children and young adults; in the absence of other pathology, it's generally assumed to be benign.[16] But joint hypermobility syndrome (JHS) has been defined as joint hypermobility in the presence of additional pathologies, as outlined in the Brighton criteria.[17] Historically, there has been some disagreement about whether JHS is distinct from EDS-HT. A 1999 survey of British rheumatologists by Grahame and Bird found that 92% thought that "hypermobility syndrome" was a distinct clinical entity, but only 39% felt it was a distinct pathological entity; asked whether hypermobility syndrome and EDS-HT were one and the same, 46% answered "do not know."[18] Respondents also demonstrated a lack of consensus regarding diagnostic criteria for the syndrome, and a "handful" denied its existence altogether. In the absence of clear molecular or genetic definitions, many experts currently regard JHS and EDS-HT to be the same condition,[2, 3, 10] and that is the working assumption in this article.

While all types of EDS can involve some level of joint impairment, this symptom is most dramatic and disabling in cases of EDS-HT.[4] EDS-HT was previously described as the most benign of the EDS classifications,[19, 20] the term *benign* here referring to lethality. Such terminology may be partly responsible for the condition's disabling symptoms being largely disregarded by the medical community.[18, 21]

Resources and Sites of Interest

The Ehlers–Danlos National Foundation
www.ednf.org

Hypermobility Syndromes Association
http://hypermobility.org

Tell Me a Story: Managing Chronic Pain from Ehlers Danlos Syndrome
www.youtube.com/watch?v=RmL7ccDa99I

My Wife Had EDS and Did Not Know It!
www.rareconnect.org/en/community/ehlers-danlos-syndrome/article/my-wife-had-eds-and-did-not-know-it

"Everyone Needs Hope": She Shares Love, Loss to Rare Genetic Syndrome
www.today.com/health/everyone-needs-hope-love-loss-rare-ehlers-danlos-syndrome-2D80532770

Generalized joint laxity puts people with EDS-HT at high risk for frequent and repeated joint dislocations and subluxations,[21] which in turn can lead to early-onset osteoarthritis[2, 10] and chronic pain.

Furthermore, recent studies have found that people with EDS-HT experience a higher incidence of impaired muscle function (as evidenced by higher levels of fatigue, weakness, and pain) than control subjects.[22, 23] Some findings suggest that such impairment is caused by reduced activity and physical deconditioning resulting from chronic pain, joint disruptions, and fear of injury.[24] But other findings indicate that muscle impairment may be due to other factors,[23, 25] such as abnormalities in the muscle collagen itself.[23]

Vascular. People with VEDS are at higher risk for early death than people with other types of EDS. They are more likely to experience blood vessel and hollow viscera disruptions, including aneurysm formation, dissection, and rupture; pseudoaneurysms; and intestinal and uterine perforation.[4, 7, 26] Historically, these complications were diagnosed only postmortem, after sudden, premature death.[26] Genetic testing now affords the possibility of earlier diagnosis, allowing providers to monitor these patients for complications and to initiate timely referral to appropriate specialties.

Although people with other types of EDS generally have normal life expectancies, they too are at risk for vascular fragility and other cardiovascular concerns.[2] Echocardiograms have revealed unexpectedly high rates of aortic root dilation in the proximal aorta in patients with classical EDS or EDS-HT.[27] Further studies are needed to learn more about progression and complication rates for aortic root dilation in the EDS population. Although rare, vascular rupture can occur in other types of EDS, particularly the classical type.[26]

Pain is a common symptom in all types of EDS, and tends to be most debilitating for people with EDS-HT.[2, 9, 11, 16, 21] One theory held that in cases of EDS-HT, pain resulted from acute episodes of joint dislocation or subluxation and subsequent early-onset degenerative joint disease.[16] Findings from more recent studies suggest that EDS-HT pain is more complex, involving combinations of acute and chronic pain and sometimes leading to complex regional pain syndrome, all of which are resistant to treatment.[16, 28] One study among Dutch patients with various types of EDS found that most had chronic localized pain originating in the musculoskeletal system, with episodes of more severe acute pain related to recurrent dislocations or subluxations.[12] Overall, patients with EDS-HT experienced the most severe pain. The researchers also found evidence suggesting that the severity of EDS-related pain is related to, and exacerbated by, chronic sleep disturbances.

Autonomic. Recent research has revealed a high incidence of autonomic dysfunction in people with EDS-HT, including postural orthostatic tachycardia syndrome (POTS).[29] POTS results from an abnormal autonomic nervous system response when a person assumes a standing position. Symptoms include an increased heart rate (30 beats per minute above baseline; or a rate exceeding 120 beats per minute) that occurs within 10 minutes of standing and isn't associated with other factors such as prolonged bed rest or medications that affect vascular or autonomic response.[29, 30] Other symptoms may include lightheadedness, palpitations, fatigue, and syncope. Unlike cases of postural orthostatic hypotension, in POTS blood pressure generally remains stable.[30] POTS is often misdiagnosed as anxiety, leading to delays in diagnosis and appropriate treatment. It often manifests earlier in people with EDS-HT than in those without EDS-HT.[29] Theories for the mechanism of POTS in EDS-HT include connective tissue laxity that allows for greater vascular distension in the lower extremities when standing and impaired central sympathetic nervous system control.[29] Precipitating events include pregnancy, surgery, infections, and trauma.[29, 30] Suspected POTS is usually diagnosed by a tilt-table or 10-second stand test. The condition can be debilitating, with approximately 25% of patients eventually becoming wheelchair- or bedbound.[30]

Gastrointestinal. EDS patients have a high incidence of gastrointestinal (GI) problems, such as gastroesophageal reflux disease, gastritis, irritable bowel syndrome, constipation, gastroparesis, diverticulosis, hernia, and intestinal pseudo-obstruction.[2, 9, 10, 31] A recent survey among French patients with EDS found that GI symptoms were common, often nonspecific, and generally not life threatening.[32] But such GI conditions can be resistant to treatment and often adversely affect the patient's quality of life.[11, 32]

Gynecologic and obstetric. Women with EDS-HT have an increased incidence of dysmenorrhea,

meno- and metrorrhagia, and uterine and rectal prolapse, although fertility and pregnancy rates appear to be unaffected.[2] A recent literature review found no documented contraindications to pregnancy for EDS-HT patients.[33] Pregnancy is more complicated for women with other types of EDS. Pregnant women with known or suspected VEDS are at high risk for uterine or vessel ruptures during labor and delivery.[4, 7] Women with more severe classical EDS are at increased risk for premature rupture of membranes, perineal tears, episiotomy incision extensions, and uterine prolapse.[9] Their infants are at higher risk for premature birth, breech presentation, and neonatal hypotonia.[9]

Other manifestations of EDS vary widely among patients. Fatigue is present in most patients with EDS-HT, and may be associated with chronic pain, sleep disturbances, muscle weakness, and physical deconditioning.[16, 23, 25] There is evidence that people with EDS-HT have a high incidence of local anesthetic failure, with many reporting partial or complete failure and others reporting shortened duration of anesthetic effect.[34] This can complicate the care of such patients undergoing dental, surgical, and obstetric procedures. Compared with the general population, people with EDS have a higher incidence of adverse outcomes after surgery because of tissue and vessel friability and delayed wound healing.[6, 21] Other clinical problems prevalent in this population include chronic headache, poor coordination, temporomandibular joint dysfunction, mucosal dryness, mitral valve prolapse, Chiari malformation, and psychological distress (including depression and anxiety).[2, 10, 11]

As one patient reported recently on an EDS discussion board,[13]

> I had begged to be sent to specialists since I was diagnosed in my late forties, and was told there was no need to even send my blood to be checked for EDS type because I was not going to have children at that age and had no biological children. The doctor said it was an expensive test, I likely didn't have the Vascular Type because I was still alive. No one saw any reason to send me to an EDS specialist, especially since most of the local doctors before iPads came out thought I was making this up and when I spelled it for them, few wrote it down.

For those who do receive a diagnosis from a knowledgeable clinician, it can be discouraging to learn that there is no definitive treatment and that symptom management is challenging and unpredictable. Geneticists, who often provide the initial diagnosis, generally don't address symptom management and long-term health care needs. Yet further care coordination with an appropriate, knowledgeable provider is typically lacking, and patients are left to navigate a frustratingly complex health care system on their own. Nurses can best assist these patients by becoming knowledgeable about the syndrome and by helping them to find and access appropriate health care resources.

The main goals of clinical management are threefold: to control symptoms, manage pain, and recognize and treat potentially life-threatening complications.

The primary symptoms of EDS include skin extensibility, joint hypermobility, and general tissue fragility.

CLINICAL MANAGEMENT

Clinical management is complex, and varies depending on the presentation and severity of the patient's symptoms and the type of EDS and its phenotypic expression. Managing patient expectations can be challenging. Typically, EDS patients have suffered for many years with the syndrome's physical manifestations, yet their concerns have often been dismissed by health care providers. In the aforementioned survey among British rheumatologists by Grahame and Bird, nearly half felt that the syndrome had only "minimal impact" on patients' lives, and more than half thought "reassurance only" was the most appropriate treatment.[18] Many patients with suspected or diagnosed EDS have reported humiliating and traumatizing experiences when seeking health care.

Controlling symptoms. For patients with EDS, it's crucial to maintain skin integrity and reduce the risk of wounds and breakdown. The skin should be thoroughly inspected, with documentation of any atrophic or atypical scars or bruises. Given the fragility of the patient's tissues, if wound sutures are needed, they must be placed with special care. Because wound healing may be prolonged, stitches should be left in place twice as long as usual.[2, 9] The use of skin tape may help prevent excessive stretching of the scar.[9] Special intraoperative care with retraction, ligation, vessel repair, and tourniquet application is necessary to prevent tissue and vessel complications.[6] Clinicians should also consider preoperative cardiac evaluation with echocardiogram before any surgical procedure.[6]

Emergency Information for VEDS

Arterial Rupture Is the Most Common Cause of Sudden Death

- Arterial or intestinal rupture commonly presents as acute abdominal or flank pain that can be diffuse or localized.
- Spontaneous arterial rupture is most likely to occur in a person's twenties or thirties, but can occur at *any* point in life.
- Cerebral arterial rupture may present with altered mental status and be mistaken for drug overdose.
- Midsize arteries are commonly involved.

Arterial, intestinal, or uterine fragility or rupture usually arise in VEDS, but should be investigated for *any* EDS type.

Carotid–Cavernous Fistula: Life-Threatening Emergency

Redness, pain, and prominence of one or both eyes and the sound of pulsations in the head can be manifestations of a life-threatening carotid–cavernous fistula:

- High-pressure blood from the internal carotid artery can shunt blood inappropriately into the tissue around the eyes and into the eye itself, causing the symptoms.
- The life-threatening risk is that the high-pressure blood will leak out of the confines of the blood vessels.

Seek immediate hospital-based medical attention, and inform emergency medical staff of the patient's VEDS and the critical risk of a carotid–cavernous fistula.

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It's also critical to maintain mobility and reduce the risk of musculoskeletal complications. Patients must avoid excessive stretching; joint hyperextension (for example, "locking" the knees while standing[10]); and demonstrating joint laxity (performing "tricks"), which should only be done at a clinician's request during a diagnostic evaluation. Patients should also avoid excessive or repetitive heavy lifting and high-impact contact sports.[6, 10] Although surgery isn't contraindicated, it's important for both clinicians and patients to recognize that, in patients with joint hypermobility, dislocations and subluxations often respond poorly to operative stabilizing procedures.[2, 6]

People with EDS should consider moderate aerobic and light resistance training to improve muscle function, fatigue, and overall quality of life.[10] If physical therapy is prescribed, it must be tailored to accommodate their greater-than-average range of motion and higher risk of injury. Physical therapy should target muscle strengthening, proprioception, gait training, and trunk stability.[16, 35] Further research is needed to determine the efficacy and long-term outcomes of various physical therapy modalities in this population.

Nurses must use caution when moving patients with EDS (particularly if they're unconscious or sedated), taking care to support all joints in positioning. Extra pillows or bolsters may be needed to support loose joints, or to maintain joints in neutral positions when appropriate. Nurses must be extremely careful when performing passive exercises on patients, so as not to hyperextend joints. If a patient uses splints or braces, it's important to check the skin frequently and thoroughly, and to pad as necessary to prevent breakdown.

Many patients will require close monitoring during ambulation. The home environment may need modification in order to prevent falls and encourage walking. Some patients may require mobility aids on a temporary or permanent basis. Care must be taken with crutches and canes, as their use can lead to upper-limb trauma and lower-limb deconditioning.[2] Patients with severe impairment may eventually need to use wheelchairs or motorized scooters, intermittently or continuously, to ensure mobility. Some patients might also need to consider using adaptive aids such as reachers, toilet seat risers, and ergonomic equipment designed for personal and household tasks.

Patients with POTS tend to experience instability in their heart rate and blood pressure with movement, and can be prone to lightheadedness and fainting. Generally, EDS-related POTS is treated by avoiding rapid position changes, using compression garments, increasing water and sodium intake, and avoiding triggers such as prolonged sitting or standing, excessive heat, alcohol, and large meals.[10, 30] The use of antihypotensives such as midodrine (ProAmatine) or an adrenocortical steroid such as fludrocortisone may also be warranted.[10]

Patients with GI symptoms may benefit from a thorough GI evaluation, and treatment as needed for conditions such as gastroesophageal reflux disease, gastroparesis, or irritable bowel syndrome.[32] Patients with such conditions should be encouraged to eat small, frequent, nutritious meals to meet their metabolic and nutritional needs. Pharmacotherapy with H_2-antagonists, proton pump inhibitors, or promotility agents may be indicated for upper GI symptoms; antispasmodics and antidiarrheals or laxatives may be indicated for irritable bowel syndrome.[10] Laxatives may also be indicated for patients on opioid therapy for pain. Patients with chronic intestinal pseudo-obstruction and other severe GI conditions may require a therapeutic course of enteral or parenteral nutrition.[31]

Pediatric patients. School-age children may require adaptations to the school environment. For example, they might need additional rest breaks and adapted physical activities. They might need to use rolling backpacks and school elevators to help protect their joints, or have greater access to snacks and drinks to manage POTS. The Ehlers–Danlos National Foundation offers a free guide to help parents and teachers

better meet the needs of school-age children with EDS (see http://bit.ly/1EvZPh5).

Managing pain. Historically, pain has been underrecognized and undertreated in people with EDS. Pain is highly variable in this population, and may involve different types and severity levels in several areas at the same time. Chronic, widespread musculoskeletal pain, particularly in EDS-HT, plays a major role in the deterioration of quality of life.[2, 16, 22] One study found that pain and its impact on daily life ("life interference") were significantly worse in patients with EDS-HT than in those with rheumatoid arthritis.[22] Many patients with EDS-HT report severe pain that is insufficiently managed by analgesics.[21] Indeed, patients with EDS often feel that clinicians don't appreciate the severity of their pain because there is no clearly defined cause. Some clinicians treat these patients as if they are drug seekers or malingerers, or are suffering from a psychiatric condition such as conversion disorder.[15, 36, 37]

Pain in this population frequently begins as episodic, mild to moderate pain related to acute injuries such as dislocations or subluxations.[2] Pain control at this point is similar to that for acute pain in any patient, and may involve rest, limb stabilization, and the use of analgesics such as acetaminophen, nonsteroidal antiinflammatory agents, or short-acting opioids.[2, 10, 16] Additional pharmacologic measures might include a course of corticosteroids and muscle relaxants.[16]

Over time, many patients with EDS develop chronic pain syndrome. The precise mechanism is unclear but may be related to repeated joint trauma and soft tissue injury, deconditioning, chronic sleep disruption, and primary abnormalities of connective tissue surrounding nerves.[12, 16] Chronic pain, most common in people with EDS-HT, is characterized by moderate to severe joint pain and myalgias. The pain is typically localized in the neck, limbs, shoulders, and hips; but the head, back, abdomen, and pelvis can also be involved. Chronic EDS-related pain may feature unpredictable exacerbations and remissions.[16]

Management of chronic EDS-related pain requires multiple modalities to provide adequate relief. Besides the first-line medications for acute pain described above, additional drugs might include cyclooxygenase (COX)-2 inhibitors such as celecoxib (Celebrex), tramadol (Ultram, ConZip), some types of antidepressants, and pregabalin (Lyrica) or gabapentin (Neurontin, Gralise).[10, 16] Although the use of opioids for nonmalignant chronic pain is controversial, in the absence of effective alternatives, providers feel justified in using opioids to treat moderate to severe chronic pain. But despite these pharmacotherapies, many patients with EDS-HT continue to find their pain debilitating.[2]

For such patients, additional pain relief modalities must be employed. Other measures that may be effective include myofascial release therapies, treatment of sleep disorders, and prolotherapy.[10, 16] Chiropractic adjustment may be helpful in some cases but must be performed with extreme caution to avoid dislocations or subluxations.[10] Patients seeking relief from EDS-related pain have reported varying degrees of success with gentle exercise, the use of braces and splints, topical and local injections of anesthetics and steroids, acupuncture, hydrotherapy and warm soaks, transcutaneous electrical nerve stimulation, massage, cognitive behavioral therapies, and meditation.[2, 10, 16, 21]

People respond to pain relief measures differently; no single modality will work for everyone. It's important that nurses document pain levels, and talk with the patient to learn what she or he typically does to reduce pain. Nurses can also help the patient to explore and evaluate various other modalities that, in combination, might provide sufficient pain relief and a better quality of life.

Recognizing and treating potentially life-threatening complications. People with EDS, particularly those with VEDS, have a high incidence of vascular and visceral complications, including fatal vessel and organ rupture.[4] All patients with known or suspected EDS should receive a baseline echocardiogram[10]; because the aorta is "especially susceptible to aneurysm and dissection formation" in this population, some EDS specialists recommend repeating the echocardiogram every one to three years.[38] For patients with known or suspected VEDS, the administration of β-blockers may be considered.[39]

Although patients with EDS, particularly those with VEDS, are at high risk for perioperative complications, some experts believe that if the surgeon has experience in working with EDS patients, the potential benefits of early correction of known defects can outweigh the surgical risks.[40, 41] For guidance regarding the recognition and treatment of spontaneous arterial rupture and carotid–cavernous fistula, both of which are life threatening, see *Emergency Information for VEDS*.

ON THE HORIZON

It's encouraging to see evidence in the recent medical literature indicative of the physical and psychosocial difficulties of people with EDS. But to date, such evidence comes primarily from case studies, studies among subjects chosen for their availability, and studies exploring specific treatments offered by the authors. And as noted earlier, because of diagnostic delays, the pool of subjects has disproportionately included patients who are more symptomatic. Larger trials involving subjects who are more representative of the EDS population are needed.

As the health care community gains awareness of EDS and experience in treating these patients, opportunities for research aimed at better defining the syndrome's clinical, genetic, and genomic bases will increase. People with EDS are desperate for evidence-based treatments to help them manage their often-debilitating symptoms, so further research into pain

management, mobility preservation, and tissue protection is vital. Research is also needed to clarify the economic impact of EDS on both the health care system overall and patients and families, especially in light of delayed diagnoses and earlier-onset disabilities. ▼

For 61 additional continuing nursing activities on physical assessment/diagnostic topics, go to www.nursingcenter.com/ce.

Linda K. Anderson is a retired RN in Seattle. She worked for seven years at a community hospital and for 27 years at an academic medical center before taking early retirement as a result of Ehlers–Danlos syndrome–related mobility issues. Contact author: lkkanderson@gmail.com. *The author and planners have disclosed no potential conflicts of interest, financial or otherwise.*

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