ARTICLE

Orthopaedic Management of the Ehlers–Danlos Syndromes

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The role of orthopedic surgery in Ehlers–Danlos syndrome is inherently controversial, opaque to most patients and many medical providers, and difficult to discern from available medical literature. Non-operative treatment is preferable, but for carefully selected patients, specific joint stabilization and nerve decompression procedures can provide symptomatic relief when conservative measures fail.

KEY WORDS: orthopedic surgery; Ehlers–Danlos syndrome; joint stabilization; nerve decompression; musculoskeletal treatment

How to cite this article: Ericson Jr. WB, Wolman R. 2017. Orthopaedic management of the Ehlers–Danlos syndromes. Am J Med Genet Part C Semin Med Genet 175C:188–194.

INTRODUCTION

Ehlers–Danlos Syndrome (EDS) is a connective disorder that in the orthopedic realm involves joint hypermobility (JH). JH is not always painful, but if so, (1) is difficult to diagnose without highly specialized training, (2) does not show on standard diagnostic tests, (3) does not respond to standard treatment protocols, (4) lowers the threshold for associated joint injuries, (5) causes premature wearing of joints, and (6) results in a higher failure rate for treatment, both medical and surgical.

EDS is often either not diagnosed or misdiagnosed, and the situation can be extremely frustrating for the patient as well as the physician and other caregivers. In spite of this, there is much that can be done for EDS patients. The role of the musculoskeletal specialist (e.g., orthopedic surgeon, physiatrist, rehabilitation medicine specialist, rheumatologist) in the care of EDS patients is to help determine the cause of the patient's complaints, and recommend treatment, based on the specific musculoskeletal diagnosis or diagnoses. It is extremely important for the physician to understand the context in which the joint problem occurs, and that the physician understands the individual patient's specific needs and expectations. This requires a thorough understanding of the bodily manifestations of EDS as well as extensive knowledge of the pathophysiology other painful conditions that cause similar, overlapping symptoms, and appreciating how these problems are affecting the individual person being treated.

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The authors have extensive experience with patients with JH issues, and the following is a brief summary, describing a general approach to patients with EDS and JH. The authors do not specifically endorse, approve, recommend, or certify any specific procedure or technique, and provide these opinions for general information only. Such information should not be considered medical advice and is not intended to

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DOI 10.1002/ajmg.c.31551

Article first published online 13 February 2017 in Wiley Online Library (wileyonlinelibrary.com).

replace consultation with a qualified physician. Complex musculoskeletal problems may best be served by a Multi-Disciplinary Team (MDT) approach including physicians (surgeons, rheumatologists, pain consultants), physiotherapists, occupational therapists, psychologists, and nurses. A coordinated team can help to plan management more effectively and can include a comprehensive inpatient (or outpatient) pain management program.

MEDICAL LITERATURE

There is sparse information in the medical literature regarding the role of orthopedic surgery in patients with EDS, particularly successful surgery. For example, a recent review article on EDS in the Journal of Hand Surgery discusses the presentation of patients with EDS and reviews the phenotypes, but does not discuss any surgical procedures that might be appropriate for patients with EDS [Christophersen and Adams, 2014]. Many journal articles refer obliquely to the higher rate of complications, treatment failure, and patient/provider dissatisfaction with surgical intervention [Freeman et al., 1996] but often lack detailed analysis or explanation of why surgery did not go well [Weinberg et al., 1999]. Under the best of circumstances, it would be difficult to form discrete, reliable generalizations about the role of orthopedic surgery in EDS patients from the available medical literature. Determining the correct and complete diagnoses in an EDS patient can be a difficult task, and the risks of all of the known hazards of surgical intervention are distinctly higher in EDS patients.

The multiple forms of EDS also have widely varying clinical manifestations [Shirely et al., 2012], and there is inherent genetic heterogeneity that further complicates any attempt at abstraction of published data. There is also considerable unfamiliarity among medical professionals regarding the clinical history, physical exam, diagnostic testing, treatment, or long-term implications of joint instability. And, unfortunately, diagnosing joint instability is not something that can be learned from medical literature or online courses; one must be educated by a hands-on approach, with direct physical contact.

Not all JH is related to EDS, and there is controversy regarding labeling EDS patients with their specific phenotype. It would be helpful in terms of tracking patients and further determining likely patterns of associated clinical problems to know their exact genetic group, but, in a practical sense, one must still deal with the involved painful joints, whether or not the group or subgroup is known. Labeling patients can increase their fear and anxiety, particularly when unfiltered information is freely available on the internet, and once labeled, the resulting bias can cause misinterpretation of subsequent symptoms by treating physicians for other conditions that may not be related to EDS.

BASICS

The medical term for partial dislocation of a joint is "subluxation," and EDS patients have frequent subluxation and occasional dislocation of large and small joints. The asymmetric loading of the joint surfaces as the joint subluxes contributes to the early wear of the joint surface, and it takes very little injury to make a "loose" joint "loose and painful." At least some of the pain is from stretch receptors near the joints, and/or from swelling of the lining of the joints. This source of pain is not reflected by diagnostic studies, at least in the early stages, and physical examination for joint instability is not routinely taught outside of orthopedics, and is not taught consistently for all joints within orthopedics.

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In a sense, EDS causes premature aging of the musculoskeletal system. Many of the musculoskeletal problems that can afflict anyone, if they live long enough, occur simultaneously in EDS patients, at an earlier age, and unfortunately also tend to cause overlapping symptoms. It can be particularly challenging for a physician to "disambiguate" the root cause(s) of the patient's symptoms.

EDS patients often have nerve pain, presumed to be related to traction and/or compression of the peripheral nerves. This type of nerve problem does not typically damage the nerves, but causes pain where the nerves end, not where they are compressed, and unfortunately does not show on electrodiagnostic tests, and can be refractory to treatment. Referred pain from nerve problems can mimic joint pain from instability, and this feature of EDS/JH seriously complicates the lives of EDS patients and their physicians.

CLINICAL PRESENTATION

EDS patients tend to present with multiple complaints, specifically vague, intermittent pain involving the limbs or spine. Doctors have a tendency to seek a simple, single diagnosis or unifying approach (the invocation of Occam's Razor), such as a attributing joint pain to a "sprain," even when there has been no injury per se, or invoking the label "fibromyalgia" when there is widespread pain. As the treatment fails, and diagnostic testing become more exhaustive but remains negative, patients often drift between different specialists—rheumatology, neurology, orthopedics, pain management—without a firm diagnosis or successful treatment plan. Patients with EDS have increased rates of

clinical depression [Berglund et al., 2015], which can seriously complicate physician and patient interpretation of strictly subjective complaints. Patients with EDS are often labeled as the problem, rather than their arm or leg. Physician burnout (emotional exhaustion, depersonalization, and low job satisfaction) in orthopedic surgeons is endemic in the United States [Daniels et al., 2016], and is likely to have more of an impact on EDS patients, with their numerous, unexplained symptoms, and seemingly unsolvable problems.

Successful surgery in general depends on the correct diagnosis (or in the case of EDS patients, diagnoses), establishing realistic expectations, and superlative technical expertise. In EDS patients, it tends to be much harder to determine the exact cause or causes of the patients' pain, expectations of the patient and/or physician may be unrealistic, and technical difficulties can have much more serious consequences. In spite of this, for patients with painful instability of joints or peripheral nerve compression, surgery may be the only treatment that reliably results in persistent pain relief.

PAIN RELIEF

Pain relief is a clear goal of every EDS patient. Surgery is often the last resort for EDS patients, and may be the only reasonable option for some conditions, such as wrist or thumb instability, but also may not be an option at all. For example, the tissues around an unstable joint may be so lax that NO surgical procedure will ever be successful. EDS patients have a higher incidence of bleeding complications, and wider scars, and less predictable healing. This does not mean they should not have surgery, but optimal treatment would include involvement of a surgeon with knowledge and experience specifically with EDS patients. Managing patients prior to considering surgical intervention is best performed by a comprehensive, multifaceted approach to care delivered by knowledgeable EDS providers.

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NON-SURGICAL TREATMENT OPTIONS FOR EDS PATIENTS

Generally speaking, non-surgical options for treatment of joint pain should be exhausted prior to recommending surgery. The following is a partial list of treatments that may help avoid the risks of surgery.

Acute Pain

Pain may be from an acute event, or a chronic pattern. In the acute setting, the standard orthopedic "R-I-C-E" (Rest, Ice, Compression, Elevation) treatment is safe and can be effective. It is not particularly effective or practical in the chronic setting. Associated joint injuries such as anterior cruciate ligament and meniscal tears in the knee, labral and rotator cuff tears in the shoulder, wrist instability, thumb joint subluxation, labral tears in the hip, and lateral ankle ligament tears are much more common in the EDS patient population; the usual treatment options for any patient with an acute musculoskeletal injury are appropriate for most EDS patients.

Chronic Pain

In the chronic setting, there are multiple options that may be effective. Patients and physicians would both appreciate an "oral medication" that results in effective pain relief, especially when diagnostic testing is normal but patients are obviously suffering. EDS patients often have multiple joints that are sore simultaneously, and a medication that reduced pain in all sore joints would be beneficial and desirable. Unfortunately, oral medication for EDS patients is problematic: Medications do not change the underlying cause of the pain, and often have side effects that negate their efficacy.

EDS patients often have a high incidence of gastroesophageal reflux [Castori, 2012], and often cannot take non-steroidal anti-inflammatory drugs (NSAIDs), or require a second medication (e.g., acid blocking, acid reducing, or antihistamine) to protect the stomach. Acetaminophen does not irritate the stomach, but is often insufficient for pain relief, and large doses can be toxic to the liver [Fontana, 2008]. Chronic use of opioid medications tends to result in tolerance and patients are at risk for dependence. Opioids are also central depressants, and tend to make postural issues worse, and can result in "central sensitization," where normal physical stimulus becomes interpreted as painful. There is also a growing legislative trend to restrict or suppress doctors from prescribing narcotics, owing to the recent rapid increase in fatal overdoses. Gabapentin and Pregabelin are similar and also anxiolytic, but associated with weight gain. Naltrexone has been used off-label for chronic pain with some success [Younger et al., 2014].

"Splints" can be quite helpful for specific types of joint instability. Several splint manufacturers make braces for most large joints, including the spine, which can be extremely helpful as part of a coordinated treatment program. Splints limit joint motion, and can therefore limit pain, but may or may not result in increased stability, and if used consistently can make muscles weaker through disuse. Special purpose finger splints are particularly effective for "Swan Neck" hyperextension deformities of the finger proximal interphalangeal (PIP) joints, and can also be effective in many patients for the thumb metacarpal–phalangeal (MP) and carpal–metacarpal (CMC) joints.

"Physical therapy" and "exercise" programs are essential components to successful pain relief in patients with

EDS (See also "The Evidence-Based Rationale for Physical Therapy Treatment of Children, Adolescents and Adults Diagnosed With Joint Hypermoblity Syndrome/Hypermobilie Ehlers–Danlos Syndrome" by Engelbert et al., this issue). Exercises that emphasize low-impact, isometric and eccentric strengthening, proprioception, and improved posture can be extremely helpful. Physical therapy can be used effectively to increase core muscle strength, and to stabilize specific joints such as the spine, shoulder, and knee. Exercise programs, often self-directed, that do not take into account that EDS patients have loose joints but tight muscles are doomed to failure. Exercise programs that emphasize "range of motion" exercises or repetitive, forceful actions such as "work hardening" are inappropriate and can make patients' joint symptoms worse.

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"Local anesthesia" injections can be helpful in determining the source of pain. It should be noted that the most common forms of local anesthesia, xylocaine, and bupivacaine, are now known to be specifically and highly cytotoxic to chondrocytes [Chu et al., 2010], and ropivacaine should be used preferentially for intra-articular injections. EDS patients are often resistant to lidocaine and bupivacaine [Hakim et al., 2005], a fact underappreciated by most physicians. Anecdotally, carbocaine tends to work better in EDS patients.

"Dietary considerations" are becoming more important and the so-called "anti-inflammatory" diets are in vogue these days. There may be clearer indications for specific dietary recommendations in the future. "Weight control" is a major imperative for any patient with EDS. "Bone health," with adequate calcium intake and appropriate vitamin D levels, is very important. Exercise is also an important component of bone health, but is problematic as physical activities can easily exacerbate pain related to instability.

SURGICAL TREATMENT OPTIONS FOR EDS PATIENTS

EDS patients are at increased risk from any form of surgery, and the outcomes are less predictable. The decision to recommend an orthopedic operation needs to be carefully considered, ideally through close collaboration between the patient, the musculoskeletal physician, the orthopedic surgeon, and the multidisciplinary team.

Surgery is an option for a select number of specific conditions in EDS patients, but there remains very little in the surgical literature to support this approach. The rate of failure of surgical intervention is clearly higher in EDS patients, particularly for conditions where ligaments are repaired, but another cause of failure is the fundamental assumption errors that are made during the diagnostic process. That is to say, the cause of the patient's pain was something other than what was operated on. In the opinion of one author (Ericson), this is particularly true in the upper extremity. This type of error is more likely to occur when the patient and his/her concerns are not the complete focus of the medical appointment.

In spite of this, EDS patients have multiple problems for which surgery may be the only reasonable option, if the diagnosis can be made correctly. With upper extremity surgery, at least in one author's experience (Ericson), most EDS patients do not have significant problems with wound healing or bleeding. Scars tend to be wider, so smaller incisions are advisable. Joint stabilization procedures in EDS patients have a higher rate of recurrence of instability, but it is lower for non-weight bearing joints such as the wrist and thumb. The lower extremity is less forgiving. Normal diagnostic tests and a higher failure rate should not preclude surgical intervention in the EDS population, but serious prudence is advised.

Cervical Spine

Craniocervical instability and Arnold–Chiari malformation may absolutely require surgical intervention. Upright MRIs are advisable when evaluating the cervical spine. Cervical spondylosis is common, and discectomy and fusion may be necessary. However, making one segment of the spine rigid tends to increase the load at each end of the fusion site, and "next-segment" disease has a much higher incidence in patients with JH. Minimally invasive techniques, when appropriate, are preferred. JH is a relative contraindication for artificial disks.

Thoracic Outlet

Thoracic outlet "symptoms" are common in EDS patients, and are often related to Thoracic Outlet Syndrome (TOS). The thoracic outlet is the space where nerves and blood vessels to the arm pass from the neck/chest area into the arm. The nerves in this area are subject to compression from the anterior scalene and pectoralis minor muscles, and the 1st rib. They are also subject to tension from inferior shoulder subluxation in patients with JH (causing thoracic outlet "symptoms" related to posture and joint laxity). Compression and/or tension on the nerves in this area cause symptoms where the nerves end, not where they are pinched or pulled. The result is vague hand/arm pain that unfortunately overlaps with the other areas that tend to be painful in patients with loose joints. Physical therapy is essential for this condition. Botox injections into the anterior scalene or pectoralis minor muscles can give tremendous relief if the patient has

TOS. Surgery may be indicated in recalcitrant cases, but detaching stabilizing muscles in loose-jointed patients can definitely make patients worse. TOS is an inherently complex and controversial topic in the medical community [Moore, 1986; Parker and Parker, 2002; Wehbe, 2004; Illig et al., 2013] and seriously complicates the lives of many patients with EDS.

Shoulder

Shoulder instability is a very common problem in EDS patients, but fortunately responds well to physical therapy in most patients. The goal of therapy is to increase the resting tone of the rotator cuff muscles, without overpowering the deltoid, which can cause bursitis and/or impingement. Radiographs and MRI are typically normal. Surgery in the form of a Neer Inferior Capsular Shift can be extremely helpful in stabilizing the shoulder [Neer and Foster, 1980; Pollock et al., 2000]. Possible complications include recurrent instability, and joint stiffness. In patients with very, very loose shoulders this procedure has a high failure rate and should be approached cautiously.

Rotator cuff and labral tears are not uncommon and are more likely in patients with excess joint motion. Surgery is indicated for full thickness tears that remain painful. Possible complications include recurrent tears and joint stiffness.

Elbow

Both lateral and medial humeral epicondylitis are more common in EDS patients. Radial tunnel syndrome is also very common in EDS patients. These problems often resolve spontaneously or with physical therapy or other modalities, such as Platelet Rich Plasma (PRP) injections [Rabago et al., 2009; Glanzmann and Audigé, 2015], but when persistent and refractory to other treatment modalities, surgery can be a reasonable option. Literature support is lacking. Posterolateral rotatory instability of the elbow may also be an issue in patients with JH and EDS.

Wrist

Wrist pain is a common complaint in EDS patients. EDS patients tend to have unstable ankles, knees, and hips, and frequently fall on their outstretched hands. This wrist trauma can convert loose wrist joints into painful loose wrist joints. Physical therapy and hand exercise often make this type of wrist pain worse. Surgical stabilization of the wrist works reasonably well for radiocarpal, midcarpal, and distal radioulnar joint instability [Büchler, 1996]. Intercarpal fusions have a role, but can create load imbalance and loss of motion that can also be painful. Painful instability of the pisiform is common, and responds well to surgery. Proximal median nerve entrapment causes intermittent severe wrist pain with pronation, and can be treated successfully with surgery if the diagnosis can be made.

Thumb

Thumb problems are almost universal in EDS patients. A painful unstable non-arthritic thumb CMC joint can be stabilized surgically, with a good prognosis [Eaton and Littler, 1973]. Unfortunately, radiographs do not correlate with symptoms [Hoffler et al., 2015], and patients must be examined carefully by specialists with extensive subspecialty training. Thumb MP joint hyperextension instability can be treated with soft tissue stabilization and/or extensor pollicus brevis tenodesis, or more reliably with arthrodesis. Painful clicking at the thumb interphalangeal joint is caused by sesamoiditis, and is treated with sesamoidectomy.

Fingers

Hyperextension of the proximal interphalangeal joints of the fingers is common in EDS patients. This may be entirely asymptomatic. If painful, or if the fingers catch or lock because of this, digital Figure-of-eight splints are extremely helpful. Surgery is an option if the splints fail, but this type of surgery is technically challenging and has a higher failure rate. Tendinopathies that can occur in anyone [Adams and Habbu, 2015] can also be present in EDS patients, and respond well to surgery, if necessary and the diagnosis is correct.

Lumbar Spine

Lumbar spondylosis is common, and spine surgery in terms of laminectomy or fusion is not uncommon. Cauda Equina Syndrome is a concern for any patient with EDS or JH who presents with severe back pain and radicular symptoms, particularly with leg weakness or perineal numbness, incontinence or sudden onset of sexual dysfunction. This can require emergency surgery to prevent permanent paralysis and loss of bladder/bowel control.

Hip

Hip pain is common in EDS patients. Lateral hip pain is common and may occur as a result of the iliotibial band subluxing over the greater trochanter. This often produces a painful, loud clunking sensation (which the patient often interprets as the hip dislocating). This can lead to trochanteric bursitis which makes if difficult for patients to sleep on their sides. This may show edema in the bursa on MRI, and usually responds to physical therapy and steroid injections (which should be avoided if possible). In recalcitrant cases, endoscopic surgery can give tremendous relief, if the diagnosis is correct [Redmond et al., 2016]. Labral tears are much more common in EDS patients, and hip arthroscopy to remove or repair this type of tear can give tremendous relief of pain, although long term evidence for this procedure is lacking. Sacroiliac (SI) joint instability is very common in EDS patients, and presents as vague low back/pelvic pain. This often responds well to physical therapy, if the diagnosis is made. Prolotherapy for isolated SI joint instability can be helpful but remains controversial. Braces to stabilize the SI joint can be helpful for episodic pain. Surgery for SI joint instability is rarely necessary but can give immediate and permanent relief of pain. Hip pain may

also be radicular pain from disk failure at L4–L5. If the radiographs and/or MRI of the hip are normal, the pain is likely referred pain from the lumbar spine. In this setting, if the lumbar spine is normal, the patient could also have Piriformis syndrome, which usually responds to physical therapy or chiropractic are if the diagnosis is made.

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Knee

Knee instability is common in EDS patients, particularly patella subluxation or patella dislocation. This usually responds to physical therapy and occasionally requires a knee support. This can eventually lead to premature patellofemoral arthritis. This excess motion at the knee can also results in a much higher incidence of meniscal tears and ligament tears. Surgery can be utilized in these cases to restore the anatomic relations. Physical therapy can be quite helpful in creating dynamic stability of the knee joint. Advances in implant design have made surgery a more viable option for patellofemoral arthritis [Shaner and Lonner, 2015].

Ankle

Ankle instability is a common problem with EDS patients. The ankle tends to give out on uneven ground, and often causes falling. The ankle may also be injured by the fall, and can become more unstable. Ankle braces and orthotics work reasonably well in many patients, but are cumbersome. Soft tissue procedures around the ankle have a high failure rate, and wound problems are common. Malalignment of the hindfoot can result in imbalance that exacerbates any underlying knee, hip or back instability or malalignment. Physical therapy and orthotics are the mainstay of treatment, but talotarsal stabilization surgery can be helpful [Graham, 2015].

Foot

Bunions are common in EDS patients. If the bunion is not painful it should best be left alone. Metatarsalgia is also common. Steroid injections may seem like a good idea for metatarsalgia, but will often weaken the soft tissues and make this problem worse. Orthotics are the mainstay of treatment for foot deformities.

Nerve

Peripheral nerve problems are common in EDS patients. Decompressive surgery for peripheral nerve compression is extremely reliable if the diagnosis is correct. Unfortunately, EDS patients often present with multiple, simultaneously overlapping nerve complaints, and sorting out the cause of the nerve complaints can be tedious, time-consuming, and resource-intensive. Electrodiagnostic studies are often ordered to assess for nerve damage, but are not helpful when the results are normal, which is common. Understanding the contribution of the patient's cervical spine and thoracic outlet to their nerve complaints is advised as a starting point.

SUMMARY

EDS results in a tendency toward premature wear of all the major joints in the body, without causing diagnostic tests to become abnormal. Painful joint instability usually responds to conservative treatment. If this is unsuccessful, it can dramatically to surgical intervention, if the correct diagnosis can be made and the right patient population is selected. Peripheral nerve compression also responds well to surgical decompression, if the correct diagnosis can be made. With multiple overlapping complaints that are linked anatomically, it is no wonder that patients and providers struggle to provide answers and solutions. Successful treatment of EDS patients requires the caregivers to have extensive knowledge of anatomy and physiology, as well as treatment options, including surgery, and extensive resources in terms of diagnostic testing, physical therapy, and consultation/coordination of treatment with knowledgeable providers.

REFERENCES

Adams JE, Habbu R. 2015. Tendinopathies of the hand and wrist. J Am Acad Orthop Surg 23:741–750.

Berglund B, Pettersson C, Pigg M, Kristiansson P. 2015. Self-reported quality of life, anxiety and depression in individuals with EDS: A questionnaire study. BMC Musculoskelet Disord 16:89(1–5).

Büchler U, editor. 1996. Wrist instability. Federation of European Societies for Surgery of the Hand. St. Louis, MO: Mosby.

Castori M. 2012. Ehlers–Danlos syndrome, hypermobility type: An underdiagnosed hereditary connective tissue disorder with mucocutaneous, articular, and systemic manifestations. ISRN Dermatol 2012: 751768.

Christophersen C, Adams J. 2014. Ehlers–Danlos syndrome. J Hand Surg 39:2542–2544.

Chu CD, Coyle CH, Chu CT, Szczodry M, Seshadri B, Karpie JC, Cielalk KM, Pringle EK. 2010. In vivo effects of a single intra-articular injection of 0.5% bupivacaine on articular cartilage. J Bone Joint Surg Am 92:599–608.

Daniels AH, DePasse JM, Kamal RN. 2016. Orthopaedic surgeon burnout: Diagnosis, treatment, and prevention. J Am Acad Orthop Surg 24:213–219.

Eaton RG, Littler W. 1973. Ligament reconstruction for the painful thumb carpometacarpal joint. J Bone Joint Surg Am 55:1655–1666.

Fontana RJ. 2008. Acute liver failure including acetaminophen overdose. Med Clin North Am 92:761–794.

Freeman RK, Swegle LE, Sise MJ. 1996. The surgical complications of Ehlers–Danlos syndrome. Am Surg 62:869–873.

Glanzmann MC, Audigé L. 2015. Efficacy of platelet-rich plasma injections for chronic medial epicondylitis. J Hand Surg Eur Vol 40:744–745.

Graham ME. 2015. Extra-osseous talotarsal stabilization: An overview. Podiatr Manage: Innov Podiatr Surg 105–113.

Hakim AJ, Grahame R, Norris P, Hopper C. 2005. Local anesthetic failure in joint

hypermobility syndrome. J R Soc Med 98:84–85.

Hoffler CE, Matzon JL, Lutsky KF, Kim N, Beredjiklian PK. 2015. Radiographic stage does not correlate with symptoms severity in thumb basilar joint osteoarthritis. J Am Acad Orthop Surg 23:778–782.

Illig KA, Thompson RW, Freischlag JA, Donahue DM, Jordan SE, Edgelow PI. 2013. Thoracic outlet syndrome. London: Springer-Verlag.

Moore M, editor. 1986. Thoracic outlet syndrome. Clin Orthop Rel Res 207:2–36.

Neer CS, Foster CR. 1980. Inferior capsular shift for involuntary inferior and multidirectional instability of the shoulder: A preliminary report. J Bone Joint Surg Am 62:897–908.

Parker JN, Parker PM, editors. 2002. The official patient's sourcebook on thoracic outlet syndrome. San Diego, CA: ICON Health Publications.

Pollock RG, Owens JM, Flatlow EL, Bigliani LU. 2000. Operative results of the inferior capsular shift procedure for multidirectional instability of the shoulder. J Bone Joint Surg Am 82-A:919–928.

Rabago D, Best TM, Zgierska AE, Zeisig E, Ryan M, Crane D. 2009. A systematic review of four injection therapies for lateral epicondylosis: Prolotherapy, polidocanol, whole blood, and platelet-rich plasma. Br J Sports Med 43:471–481.

Redmond JM, Chen AW, Domb BG. 2016. Greater trochanteric pain syndrome. J Am Acad Orthop Surg 24:231–240.

Shaner J, Lonner JH. 2015. A resurgence for patellofemoral arthroplasty. Int Congr Joint Reconstr. Available at: http://icjr.net/article_119_patellofemoral_arthroplasty.htm#.WJBJubHMwUE

Shirely ED, DeMaio M, Bodurtha J. 2012. Ehlers–Danlos syndrome in orthopedics. Sprts Health 4:394–403.

Wehbe M. 2004. Thoracic outlet syndrome. Hand Clin 20:119–121.

Weinberg J, Doeriing C, McFarland EG. 1999. Joint surgery in Ehlers–Danlos patients: Results of a survey. Am J Orthop 28: 406–409.

Younger J, Parkitney L, McLain D. 2014. The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain. Clin Rheum 33:451–459.