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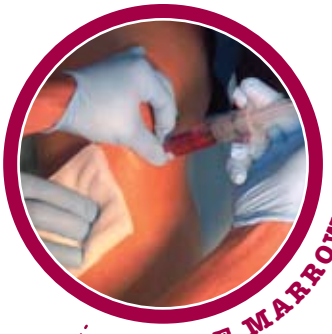

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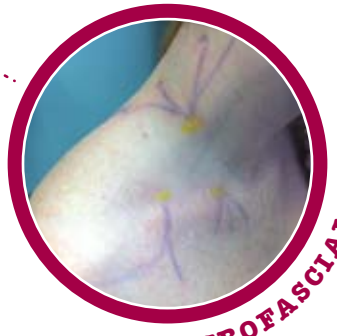

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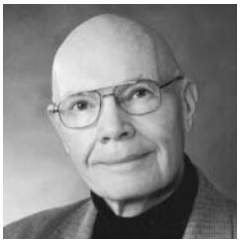

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Richard L. DonTigny, PT received his Physical Therapy certification from the University of Iowa in 1958 and his Bachelor's degree from Montana State College. For 28 years, Richard worked as a therapist in both the Colorado Springs, CO and Havre, MT areas, before heading up his own private practice for the next 10 years, working alone and unfunded to further advance his development of the dynamics of the pelvis. He retired from private practice in 1996, and continued on his path of teaching, research, and writing. Richard is a well-known lecturer and author. He has published numerous articles and book chapters, primarily on the mechanics and function of the sacroiliac joint. More on his method can be found at www.thelowback.com. How it works, why it hurts and how to fix it. Richard DonTigny may be reached at 1547 N Hunters Way, Apt 305, Bozeman, MT 59718.

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Karina Gordin graduated from Tufts University in 2007 with a bachelor's degree in English, emphasizing creative writing. In 2009 she received a Masters of Natural Products from Massachusetts College of Pharmacy and Health Sciences. Karina has officially combined both degrees to pursue medical journalism, and has since written for publications including *Townsend Letter*, *Healthcare Ledger*, *Lilipoh*, *Natural Standard database*, and *RN Journal*, among others. She is currently developing her own seasonal publication, as well as blogging on the theme of health freedom and wellness. Writing for *Journal of Prolotherapy* has undoubtedly been an unparalleled opportunity and privilege, and Karina always looks forward to collaborating with the publication to provide the kind of ground-breaking reports that can change the world. To contact Karina, email her at catspop7up@aol.com.

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Ross A. Hauser, MD received his undergraduate degree from University of Illinois. He graduated from the University of Illinois College of Medicine in Chicago and did his residency at Loyola/Hines VA in Physical Medicine and Rehabilitation. Dr. Hauser is the Medical Director of Caring Medical and Rehabilitation Services in Oak Park, Illinois and is passionate about Prolotherapy and natural medicine. Dr. Hauser and his wife Marion, have written seven books on Prolotherapy, including the national best seller *"Prolo Your Pain Away! Curing Chronic Pain with Prolotherapy,"* now in its third edition, a four-book mini series of Prolotherapy books, and a 900-page epic sports book on the use of Prolotherapy for sports injuries. Dr. Hauser may be reached at 715 Lake St., Suite 600, Oak Park, IL 60301; Tel: 708.848.7789; www.caringmedical.com.

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ADAM D. WEGLEIN, DO, DABMA

Dr. Weglein is certified in Sports Medicine, certified in Prolotherapy from the American Association of Orthopaedic Medicine, and certified-Diplomat of the American Board of Medical Acupuncture. He graduated Summa Cum-Laude from University of Texas at Arlington. He received his medical degree in Doctor of Osteopathic Medicine from the University of North Texas Health Science Center in Fort Worth. After successfully completing a family residency at the University of Texas Houston, he went on to do a Sports Medicine Fellowship at South Pointe, Cleveland Clinic, Cleveland, Ohio, and subsequently became the Assistant Program Director of the Sports Medicine Fellowship. Dr. Weglein has been a national speaker on the topic of acupuncture in sports medicine at the Annual American Osteopathic Academy of Sports Medicine, and has given many lectures on the topic of Prolotherapy, PRP and regenerative medicine. Dr. Weglein can be reached at 4295 San Felipe St., Suite 230, Houston, TX 77027; www.houstonsportsdoctor.com.

GREAT NEWS CORNER

Regenerative Medicine has Many Innovators

Ross A. Hauser, MD

Once physicians starts doing regenerative medicine or alternative medicine, they never go back to regular allopathic medicine. As I have recently studied for my recertifying exam in Physical Medicine and Rehabilitation, I was struck as to how many conditions Prolotherapy can cure where traditional treatments fail. While exercise, manipulation, manual therapies, and physiotherapy, as well as corticosteroid shots and surgery have their place, the whole field of pain medicine would be altered drastically if Prolotherapy would gain its rightful place in the treatment of joint instabilities, tendinosis, and the whole gamut of non-healing degenerative joint and soft tissue conditions. Fortunately for all of us, the field of Prolotherapy is filled with many innovators that are continually pushing Prolotherapy forward and showing us all that the body has tremendous regenerative capabilities. The next two issues of the *Journal of Prolotherapy* will be filled with the techniques and stories from these brave, skilled, and innovative clinicians.

A good friend of mine Gerardo Cajero Callejas, MD, who was one of the first doctors in Mexico doing Prolotherapy, sent the *Journal of Prolotherapy* some of his results from the headache patients he has treated at his clinic. (*See Figure 1.*) Because of his work, and that of other doctors, including Jose Eleazar Calderon, MD, Prolotherapy is gaining momentum in Mexico. Dr. Calderon combines traditional Hackett-Hemwall Prolotherapy with ozone therapy to enhance healing. In this issue, to educate us all on this technique, Frank Shallenberger, MD, the main proponent of using ozone in regenerative injection therapy, wrote an article on what he termed Prolozone™. Dr. Shallenberger also teaches courses on Prolozone™ for anyone wanting to learn the technique.

As most of us are aware, it appears that this decade is fast becoming the decade of stem cell therapy. To introduce the topic, we have included an article by someone who is doing innovative work in this field, Harry Adelson, ND. He describes the technique he is using, direct bone marrow injections, for conditions such as degenerative osteoarthritis.

Another exciting area of innovation for Prolotherapy is the work of New Zealand physician, Dr. John Lyftogt. His technique has several names including Neurofascial Prolotherapy, Neural Prolotherapy or Subcutaneous Prolotherapy, and involves the injection of 5% dextrose around the subcutaneous nerves with the purpose to promote regeneration, repair, or other functional restoration in subcutaneous nerves. His treatment helps decrease neurogenic inflammation in the small nerves that can be the source of chronic pain. He has published some impressive results on the therapy.[1-3] One of the doctors who practices this technique, Adam Weglein, DO, shares his knowledge on how to incorporate this technique into a Prolotherapy practice.

Wow, what an issue! We are also fortunate this month to have Richard DonTigny, physical therapist, give us his insight into the sacroiliac joint in the second part of his two-part series. Mr. DonTigny first published his findings in 1962. His method of analysis and treatment of the sacroiliac joint, in physical therapy circles, is known as The DonTigny Method™. At the age of 79, we are grateful that he continues to share his knowledge on the sacroiliac joint. Yes, Mr. DonTigny, we agree the sacroiliac joint moves! Another passionate Natural Medicine advocate, Karina Gordin, has submitted her Case for Prolotherapy which takes a look into the hypocrisy of what treatments are typically covered by insurance in traditional pain management, while Prolotherapy is often not covered. Thank you Karina, for your contribution and support of Prolotherapy and Natural Medicine!

Babette Galdstein, VMD continues to expand the veterinary literature on the use of Prolotherapy in animals with her case studies. To reiterate this point, for the work of Prolotherapy to become established in human medicine, it is extremely helpful to show its efficacy in animals. It is

Table 1. Patient Characteristics.

Patient	1	2	3	4	5	6	7	8	9
Sex	Male	Female	Female	Female	Female	Male	Female	Female	Male
Age	68	44	79	51	68	90	63	43	54
Job	Executive	Nurse	Home	Home	Home	Retired	Home	Home	Tinsmith
Symptoms	Headache & shoulder pain	Headache & cervical pain	Headache & cervical pain	Headache	Headache	Headache	Headache, dorsal & shoulder pain	Headache & cervical pain	Headache
Signs	Mild limitation for cervical movements	Cervical stiffness	Cervical stiffness	None	None	None	Cervical stiffness, occipital pain	Occipital pain at pressure	Shoulder pain
No. treatments	3	10	7	1	3	4	3	3	3

Table 2. Patient Results.

Patient	1	2	3	4	5	6	7	8	9
Pain	Much better	Released	100% relieved	Much better	50% improvement	Released	Much better	Released	Released

The nine patients I am presenting suffered from chronic headaches that spanned from mild to severe pain. The patients had previously been treated with several methods, including manipulation, braces, physiotherapy, NSAIDs, and other migraine drugs.

All of the patients were injected in occipital and cervical regions and received between one and 10 treatments, given every six weeks. Each were injected with a Prolotherapy solution consisting of 15% dextrose and 2 % lidocaine, using 22G, 3-inch needles. Thirty injections were given at each treatment. We prescribed them a paracetamol-like analgesic and didn't recommend excessive rest. They continued their normal activities, then started an exercise regimen after the second treatment. None of the patients used a neck brace.

Prolotherapy has demonstrated a 85% to 90% success rate in my private practice. Furthermore, Prolotherapy has prevented the patients from requiring expensive medical treatments and unnecessary surgeries. Only one patient was not satisfied with the results of the treatment because the pain only improved by 50% and she needed to continue to take some pain medications. The rest of the patients were satisfied with the results. Some of them came back to my office for pain problems in others areas of their bodies, which were also treated with Prolotherapy.

Figure 1. Results from headache patients treated by Gerardo Cajero Callejas, MD, at his clinic in Mexico.

believed that placebos don't have an effect on animals.[4] Thus, if Prolotherapy works for degenerative arthritis and other conditions in animals, this gives credence to the notion that Prolotherapy regenerates injured structures.

As with all innovation, time will tell if the various procedures work long term or not. What will be the place in chronic pain management for techniques such as Hackett-Hemwall Dextrose Prolotherapy, Bone Marrow Prolotherapy, Stem Cell Prolotherapy, Prolozone™, PRP Prolotherapy, or Neural Prolotherapy? Whatever the place, we agree that the more we publish and the better the studies that are published, the easier this question will be answered. Dr. Gary Clark gives us his insight and recommendations for those desiring to publish their Prolotherapy results in Part III of his four part evidence-based medicine series.

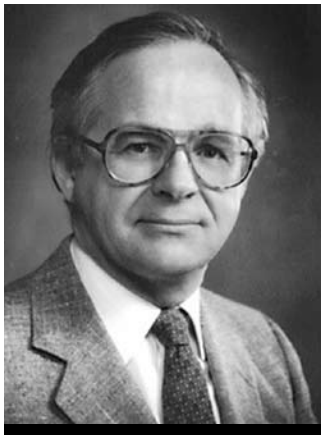
Lastly, I have co-authored a research paper with Hilary Philips on Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome. These are very painful conditions, with a lack of successful traditional treatment options. In my experience, Prolotherapy is a highly effective treatment for these conditions. Even considering these multiple joint cases, the patient cost is a fraction of surgical costs and can help patients lead active, fulfilling lives. I can only think that as we continue to document the results of Prolotherapy by good patient questionnaires, and of course, objective measures such as physical examination parameters, MRI, and ultrasound scans, that some day the vast expanse of pain management will look a lot different than it does today.

PROLOTHERAPY AND ORTHOPAEDIC MEDICINE LOSE TWO OF ITS CANADIAN PIONEERS: TRIBUTE TO DRS. JOHN E. MERRIMAN AND DONALD M. FRASER

Anyone involved with orthopaedic medicine and Prolotherapy in the United States will be familiar with the names John Merriman and Donald Fraser. Both were true pioneers and we owe them a great debt.

Dr. John Edward Merriman was awarded a lifetime achievement award by the American Academy of Orthopedic Medicine in 2005. Dr. Merriman, always an innovator, established the first cardiac rehabilitation program in North America at the University of Saskatchewan in 1962. He was a cardiologist by training and a Professor of Medicine at the university. In 1975, he moved to Tulsa, Okalahoma to establish a medical practice. At a Christian medical conference he met Dr. Gustav Hemwall and became interested in Prolotherapy. Dr. Merriman went on many missionary trips with Dr. Hemwall and other doctors utilizing Prolotherapy. He was a beloved man. I had the pleasure of working with him at a medical missionary clinic in rural Illinois. He led an amazing life. He was devoted to God, his family and his work as a physician and a researcher in Prolotherapy. He spent the last 20 years of his life doing Prolotherapy at his Tulsa, Oklahoma office. He retired in 2010 at the age of 85. He passed away peacefully with his wife and children by his side on February 7, 2011.

Dr. John E. Merriman



Dr. Donald M. Fraser

The term orthopaedic medicine in North America is synonymous with Dr. Donald M. Frasier. A gifted physician, scholar, and teacher, he practiced Family Medicine in St. Catharines, Ontario from 1953-1982. In 1983, he devoted his energy and expertise to orthopaedic medicine, for which he was internationally known and respected. He continued to see patients for 28 years, right up until he died on December 18th, 2010. It is difficult to adequately include how Dr. Fraser helped shape, promote, and further the cause of orthopaedic medicine in the United States and Canada. He was a charter member of the American Association of Orthopaedic Medicine, served on its Board of Directors, and received the 2001 Lifetime Achievement Award for his continuing work in this field of medicine. He was personally trained by Dr. James Cyriax and became a Fellow in the Society of Orthopaedic Medicine. He was a mentor to many physicians who subsequently became leaders in the field of Orthopaedic Medicine.

We are grateful to these two pioneers who helped get orthopaedic medicine and Prolotherapy established in North America. We at *JOP* are committed to carrying on their work and message. ■

Until the next injection,
Ross A. Hauser, MD

Ross A. Hauser M.D.

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LETTERS TO THE EDITOR

Letters from Clive Sinoff, MD

To the Editor,

Dr. Van Pelt has given an excellent description of prolotherapy of the foot and ankle.[1] He states that "If the tendon has a complete rupture then orthopedic surgery is required and referral will be made promptly". However, there are articles showing that conservative treatment (without prolotherapy) provides very much the same results, perhaps with a higher risk of re-rupture, but less complications, than surgery.[2,3] Consequently, it seems that even complete rupture can be treated conservatively, and prolotherapy is likely to further increase the success of non-operative treatment.

Clive L. Sinoff, M.D.

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Dear Dr. Sinoff:

Appreciate your letter. Yes, if someone was to treat it conservatively with Prolotherapy, the patient would have to be in a brace that keeps the Achilles tendon in a shortened position, with the intention of encouraging the two torn ends to reattach. On another note, Prolotherapy can of course be given after surgery. I recently had a patient completely tear his Achilles tendon and wanted to know when he could get Prolotherapy because helio skiing season was approaching. Once he was cleared at his post-op visit by the surgeon, he came in for PRP Prolotherapy. He made, what I would term, a "quickened" recovery and enjoyed the last helio skiing season without incident.

Also, in a separate email, you had mentioned the mix up in Table 1, on page 546 of the February issue, regarding the percentage of female to male patients. The table should have stated 74% female and 26% male, as it stated in the text. Thanks for pointing that out.

Ross Hauser, MD

Dear Ross,

Obtaining reliable prolotherapy studies is very difficult and your retrospective reports are invaluable. I cannot envisage prospective randomized studies in the future, and as far as I can ascertain, there are only a handful of published small randomized studies. However, I believe that it would be possible to develop convincing prospective non-randomized studies with:

1. Standardized data collection
2. A control group that does not receive prolotherapy for whatever reason—in my situation more than 90% of my patients never receive prolotherapy because of denials by Workers' Comp.

This is just a preliminary thought. Perhaps such studies could be done in conjunction with the American Osteopathic Association of Prolotherapy Integrative Medicine and the American Academy of Orthopedic Medicine. We would need someone with your expertise and drive to spearhead this. Any thoughts?

Best regards,
Clive Sinoff

Dear Dr. Sinoff:

Thank you for your correspondence. As we all know, doing controlled studies is very difficult and cost prohibitive. We are making a lot of strides in Prolotherapy research, as evidenced by the fact that so many non-Prolotherapy articles mention the word Prolotherapy. Just today, I saw it mentioned in a very prominent Ehlers-Danlos article I was reading. While I appreciate your words as it relates to studies I/Caring Medical have published, the coordination of research with a lot of different centers is not my forte. Though what you describe would be great for Prolotherapy, it would have to be someone with a research background, which few have that are involved with Prolotherapy. Let's hope someone reading this will take up the gauntlet and pursue this with your suggestions.

Ross Hauser, MD ■

IN THE SPOTLIGHT

Case for Prolotherapy

Karina Gordin, BA, MS

HR3962 guarantees quality, affordable healthcare with expanded access to "reasonable and customary" treatments, which aim to ultimately reduce the growth in health care spending. But questions remain: are the affordable, "reasonable and customary" treatments indeed of quality and will therefore reduce health care spending, or should the health care reform be reformed to include reasonable and non-customary treatments as well?

To answer these questions we needn't look further than a costly, growing epidemic like musculoskeletal disease, which affects 1 in 4 Americans today, and amounts to $849 billion in direct and indirect expenditures.[1] In fact, joint, muscle, tendon, and ligament impairments are the leading cause of disability in the United States, and are projected to increase in the next 25 years if our current medical care approach is not thoroughly reviewed and updated. According to the World Health Organization (WHO), musculoskeletal disorders are a leading cause of morbidity, and substantially influence health and quality of life, inflicting an enormous burden of cost on health care systems.[2] Even so, comprehensive research overwhelmingly points to poor results[3] exhibited by insured customary procedures, which in turn will put a greater financial strain on health care organizations in the forthcoming years.

CORTISONE

Currently, health insurers manage the scope of musculoskeletal disorders by covering customary treatments ranging from steroid injections and arthroscopic surgeries to spinal fusions, which not only cost Americans extra billions in preventable expenses, but are not well supported in double-blind studies. Dr. Richard Wrenn's experimental study investigating the effect of cortisone on the restoration of injured tendon strength and elasticity, demonstrated suppressed fibroblastic reactions (connective tissue formation) to injury following intramuscular injections of cortisone.[4] In a comparable study by Chandler et al., an intra-muscular hydrocortisone injection was shown to accelerate degenerative osteoarthritic changes of the hip joint, following 18 treatments.[5] A similar case was reported by Sweetnam et al., although only 3 injections were administered in the study. Steinberg et al. observed a Charcot-like arthropathy (joint dislocation) in a rheumatoid knee after 22 hydrocortisone injections over a 2-year period; identical changes were reported in both knees of a patient who had received a total of 52 intra-articular injections of corticosteroid over a period of 14 months. Essentially, the aforementioned variety of tissue pain and inflammation is suppressed by palliative corticosteroid injections, at the cost of decreased collagenase, and compromised prostaglandin and granulation tissue formation. Simply put, the latter collagen rich tissue must be formed by fibroblasts to heal injured sites, so suppression accounts for poor circulation and jeopardized immune cell repair processes. Because the corticosteroids block glucose uptake in the tissues, thus enhancing protein breakdown and inhibiting new protein synthesis, formation of collagen (protein) and collagen dependent cartilage is arrested.[6] A study carried out at University Central Hospital in Helsinki confirmed that even after a single steroid injection into the knee, cartilage digestion of the joint occurred, while cartilage elasticity was simultaneously reduced.[7] In a parallel study examining articular cartilage in joints, it was found that 16 weeks following a single joint injection, cartilage remained biochemically and metabolically impaired.[8] Undoubtedly cortisol and synthetic analogs may prevent or suppress the development of local heat, redness, swelling and tenderness, by which inflammation is recognized,[9] but on the microscopic level, vital processes are also prevented or suppressed, such as inflammatory cascade, capillary and fibroblast proliferation, deposition of collagen and granulation tissue (scar) formation.[10]

NSAIDS

While cortisone injections are still considered the standard of care, non-steroidal anti-inflammatory drugs (NSAIDs) are the second line of attack, typically recommended for the first three to five days following acute connective tissue injury, or ongoing administration for chronic musculoskeletal conditions. Unlike corticosteroids, this treatment is non-steroidal as the name implies, yet the main function likewise aims to reduce inflammation. By blocking the production of prostaglandins and leukotrienes,

both treatment forms mediate the inflammatory process, inhibiting blood flow to injured area, reducing protein synthesis, compromising new blood cell formation, fibroblast proliferation and ultimately collagen formation. Rashad et al. cited a study, examining the effects of NSAIDs on the course of osteoarthritis (OA), stating that synthesis of cartilage matrix component was inhibited by anti-inflammatory drugs such as sodium salicylate and indomethacin, and thus accelerating arthritic changes.[11] A retrospective study surveying patients with osteoarthritic hips suggests that NSAIDs contributed to destruction of the hip joint, confirmed by x-ray studies.[12] In another study examining the use of perhaps the most popular anti-inflammatory drug used in sports medicine, ibuprofen, in the treatment of tendon injuries, it was found that ibuprofen decreased flexor tendon strength by 300% at four weeks.[13] Unquestionably anti-inflammatory medications, like steroid injections, immediately reduce pain, offering athletes and employees quick relief and prompt return to sport or work, but such short term benefits are likely outweighed by ensuing tissue damage, including chondrocyte necrosis (cartilage cell damage) and reduction of fibroblast growth and collagen synthesis in the joint. Given that 99% of tendon by dry weight is collagen,[14] and fibroblastic growth is crucial to mechanical stability and strength of tendons and ligaments, it is unfounded to treat injured collagen with fibroblast inhibiting anti-inflammatories. Is it any wonder that adverse drug reaction (ADRs) statistics link NSAIDs to a class of drugs with the highest frequency of side-effects and deaths,[15] with incidences of adverse events accounting for an estimated 7,600 deaths and 76,000 hospitalizations in the United States?[16] Side-effect lists for NSAIDs occupy 50% of space for each drug in the *Physican's Desk Reference*,[17] with one side-effect being increased healthcare expenditures.

High costs of unsupported NSAID treatments compound the long-term economic burden of musculoskeletal disease. Between 1996-1998 and 2002-2004, the use of prescriptions rose substantially, with more then 2.3 billion prescription medications[18] filled for persons with musculoskeletal disease. The widespread use of coxibs for inflammatory conditions partly accounts for the mean annual prescription costs, which were computed in 2004 to be $653 to $1,196 per person.[19] In brief, prescription costs, along with costs associated with treating prescription side-effects comprise a substantial sum of avoidable healthcare expenditures.

Side-effect lists for NSAIDs occupy 50% of space for each drug in the *Physican's Desk Reference*,[17] with one side-effect being increased healthcare expenditures.

ARTHROSCOPIC SURGERY

Following an arsenal of NSAIDs, the classic next step to tackling non-healing injury involves a scalpel or arthroscope. The latter method, also known as arthroscopic surgery, is a therapeutic modality that serves as both a diagnostic and surgical tool. Less conservative when compared to NSAIDs and corticosteroids, surgical procedures treat pain via removal of tissue rather than removal of inflammation; all the same, cartilage repair may be stifled.[20] Common sites for such procedures include arm (and shoulder), foot and knee regions, which are frequently subject to repetitive strain, high impact fractures, over exertion, and repetitive workplace and sport related trauma. The former region accounts for 53%–59% of total fractures treated, while lower limb fractures account for 42%–48% throughout the years. In sports trauma, which accounted for 9% of impairments in 2004, the lower extremity is most commonly injured; fractures of the ankle, foot or toes accounted for more than one-half of treated lower-limb fractures. Dislocated knee joint episodes represent 63% of the 5.1 million injuries treated in 2004, with shoulder dislocations representing 6%.[21] In the event of such injuries, surgical reconstruction and arthroscopic shaving is recommended, especially when knee meniscal tearing is involved, rotator cuff strains occur, or anterior cruciate ligaments become lax.

TRADITIONAL TREATMENT OF MENISCUS & ACL INJURIES

In terms of meniscal tears, partial or full meniscectomy is commonly performed, since it is widely believed that the inner two-thirds of meniscus tissue (white zone) heal poorly otherwise.[22] However, because the meniscus functions as a shock absorber and indirectly provides nutrition to the articular cartilage, removal may interfere with nutritional support, triggering cartilage deterioration, subsequently placing excessive contact stress pressure on the bone, lessening shock absorption and potentially inducing arthritis. Numerous studies demonstrate that contact stress

pressure on articular cartilage significantly increases, following meniscal removal.[23] One such study exhibited a 110% increase in contact stress pressure following partial meniscectomy, and 200% increase following total removal. The study concluded that "the contact stresses increased in proportion to the amount of meniscus removed."[24] In an animal study, it was shown that meniscal repair may largely cause further spreading of the injury to non-injured meniscal tissue.[25] To add insult to injury, early arthroscopic complications may also be attributed to side-effects, including bleeding into the joint, infections, which account for 12.1% of complications, and thromboembolic disease (blood clots), accounting for 6.9%.[26] One study reported 30 saphenous (femoral) nerve injuries, 6 peroneal (fibular) nerve injuries, 22 infections, 3 vascular injuries, and 4 cases of thrombophlebitis (irritation or infection of blood vessels.)[27] Anterior cruciate ligament reconstruction exhibits distinct side-effects following arthroscopic procedures, such as sepsis (infection), skin necrosis, arthrofibrosis (excessive scar tissue), tourniquet paralysis, amongst other complications.[28] The most common side-effect following ACL reconstruction; however, is arthrofibrosis, engendering loss of flexion, extension, or both—an incidence shown to be as high as 3.7%.[29] This complication may be attributed to factors such as infection and bleeding into the joint, followed by immobilization (stress deprivation); further arthroscopic manipulation may be required for scar resection.[30] Supplementary complications may arise from ACL reconstruction surgery techniques involving replacement of injured ligament with prosthesis or tendon to stabilize the knee. In one five year study examining arthroscopic ACL reconstruction with patellar tendon graft, ruptures occurred in 5% of patients.[31] More over, grafts have been found to be three to four times stiffer than actual ACL's, while artificial graft particles were implicated in stimulating proliferative arthritis when injected into the knees.[32]

TRADITIONAL TREATMENTS FOR SHOULDER INJURIES

Shoulder arthroscopy is also fraught with complications including nerve injury, rotator cuff tears, as well as the hemarthrosis (bleeding into joint) and infections.[33] A possible explanation for such risks may be related to the instrumentation. Joints, which normally hold approximately 5 milliliters of fluid, are forcefully pumped with upwards of 120 milliliters of fluid to distend the joint, increase visibility and clear debris, after which large probes, shavers and pumps are inserted to trim and suture.[34] Clearly the incision site is vulnerable to infection, and considering the size of area operated on, stretching, swelling and increased sensitivity is reported.[35] Though rarer, risks like blood clots and strokes are attributed to use of anesthesia in surgery.[36]

COST BURDEN OF TRADITIONAL TREATMENTS

The high cost of customary treatment related side-effects imposes an increasing financial burden on government, our nation's fiscal future, state economy, and of course our households; after all, poor patient outcomes require follow-up treatments, postpone time off work, and increase direct/indirect expenditures, which raise growth in health care spending, and ultimately render the affordable, customary treatments costly. Particularly, in 2004 the sum of direct expenditures in health care costs and indirect expenditures in lost wages was estimated to be 7.7% of the national gross domestic product. One facet of the latter statistic relates to ambulatory care visits to physicians (direct expenditure), which accounts for a large and growing share of healthcare utilization. In any given year, at least 85% of persons with musculoskeletal disorders use this resource, averaging around six such visits per year. Between 1996-1998 and 2002-2004, ambulatory physician visits increased from 435.5 million to 507.9 million.[37] That is one example of direct expenditures of the musculoskeletal disorders burden; others include hospital inpatient and outpatient services, physician and other practitioner services, home health care, prescription drugs, and administration as well as non-health sector costs. Taking arthroscopic knee surgery into consideration, the national average price is $11,900,[38] with additional costs for rehabilitation; ambulatory surgery mean charge for arthroscopy was $8,970 in 2007,[39] while the mean charge per visit/stay in a community hospital for inpatient knee surgery was computed to be $38,674.[40] It appears that price range hinges on location and type of facility, insurance and co-pay, patient age, et cetera.

Indirect expenditures relate to mortality and morbidity, including the value of productivity losses, and value of lifetime earnings.[41] For instance, improperly treated musculoskeletal conditions present tremendous morbidity costs due to lost work days and lifelong pain that requires ongoing management. In 2005, the National Center for Health Statistics reported in its National Health Interview Survey that 1 in 6 persons (16%) employed in the previous 12 months in the US accounted for lost work

totaling nearly 437.6 million days.[42] On average, workers lost 12 days in a 12 month period, while more than 1 in 5 persons (21%) reported at least 1 bed day in the previous 12 months all due to musculoskeletal disorders, with total bed days reported at more than 810.3 million. Wage losses for persons aged 18 to 64, added in 2004 another $339 billion, or 3.1% of the GDP[43] to the total cost. Parenthetically, comparing cost of musculoskeletal disease to the GDP provides a firm perspective on the rising, preventable costs that profoundly impact our nation's economy; thus, emphasizing the need for new, quality, cost-effective treatments that will consume a less substantial portion of our healthcare resources. Since the 1996-1998 period, expenditures have grown by at least 0.4% of GDP, and are likely to continue growing more severe as a result of a graying boomer population, costly treatment approaches, lost work days, extended bed days and lost earnings. Accordingly, health care services worldwide will be facing severe financial pressures in the next 10 to 20 years due to the escalation in the numbers of people affected by musculoskeletal disease.[44]

INITIATIVES TO IMPROVE BONE AND JOINT HEALTH

To prevent this model, President George W. Bush launched a global, multi-disciplinary initiative in 2002, which primarily focuses on improving bone and joint health, reversing physical, emotional and financial demands of musculoskeletal disorders, and forestalling the projected statistics. The organization aims to accomplish its mission by developing new treatment approaches through research and educating policy makers, professionals and public, as well as increasing investment in health policy research, and finally delineating the underlying mechanisms of musculoskeletal disorders, and their response to treatments. Unquestionably, delineating underlying mechanisms is the best place to start. Connective tissue physiology as well as the etiology and pathophysiology of musculoskeletal diseases must be revisited. Better appreciation of mechanisms relating to connective tissue healing and recovery, inflammation as well as the precipitating causes of strains, sprains, tendinopathy, and lax ligaments, may compel a reassessment and subsequent overhaul of our treatment approach and thereby reduce direct/indirect expenditures, growth in health care spending, and preclude risk of adverse reactions and risk of re-injury.

To regress momentarily, studies presented earlier confirm that our current treatments effectively take for granted the body's innate response to injury by suppressing a series of actions, starting with the inflammatory cascade, which in fact play a variety of restorative roles. Hence, inflammation is closely interwoven with the process of repair.[45] The key issue is, though inflammation and proliferation equates repair, the process is slow, and that is unacceptable for a medical system that strives for immediate results. On account of poor vascularization,[46] low oxygen consumption, and anaerobic energy generation, the resulting metabolic rate of connective tissue is gradual, and healing capacity is limited[47] leading to fibrosis (formation of scar tissue), and suboptimal tissue integrity and functionality.[48] Even so, it must be noted that despite poor blood supply, *unsuppressed* fibroblasts and chondrocytes can undergo rapid division in response to a variety of stimuli, including trauma, and are therefore able to regenerate the tissue of origin, such as cartilage.[49] Connective tissue cells, like chondrocytes, fibroblasts and osteocytes, which secrete connective tissue matrix, are dormant in adult mammals; yet, they proliferate in response to injury with fibroblasts expressly proliferating widely and constituting the connective tissue growth once stimulated by inflammation. By recognizing the conflicting medical perspectives and corollary practices, a compromise is warranted, which embraces the body's fundamental regenerative capacity; yet, hastens the repair process through improved customary treatment approaches to ensure that connective tissue injuries are less debilitating, and the burden of musculoskeletal disease in America reversed.

THE ROLE OF PROLOTHERAPY

One such compromise is Prolotherapy. Non-steroidal, non-surgical, and pro-inflammatory, this "proliferative injection therapy" is founded on the fundamental understanding of connective tissue injury and healing mechanisms; in spite of the intervention's less profitable nature, when compared to current customary treatments, it seamlessly culminates the "Bone and Joint Decade" efforts to offer a cost-effective, novel, preventative and therapeutic approach to mitigating societal and personal musculoskeletal burdens. With a Western medical treatment like Prolotherapy widely available, physical and economic burdens are avoidable even if tendon, ligament and joint injuries are not, occurring unexpectedly at the workplace, on the field, at home or in collision accidents. Too often what may start off as a trivial sprain, can progress into a disabling chronic pain condition. Such as, ankle sprains are exceptionally common in the general

and athletic populations; approximately 25,000 people sprain their ankles daily.[50] If improperly handled, the sprained tissue may become scarred over, stiff and a source of ongoing pain. While the scenario in which ankle injuries occur is not uncommon, injury progression could be; in brief, total relief of such structures begins with understanding of the structures.

Ligaments and tendons are a complex of interdependent collagen, elastin, glycoproteins, protein polysaccharides, glycolipids, water and cells.[51] Collagen is the major component of the extracellular matrix, or "connective tissue," constituting approximately 25% of the protein in mammals.[52] Therefore the physical behavior of ligaments and tendons, and their healing potential depends greatly on their main component, collagen, and the ground substance of collagen fibers, water and proteoglycans. Fibroblasts synthesize the collagen and proteoglycans in muscles, ligaments, tendons and fascia; chondrocytes, which are connective tissue cells much like fibroblasts, are involved in the formation of cartilage. As noted earlier, fibroblasts and chondrocytes normally demonstrate a low level of replication; however, in response to stimuli, such as trauma, these cells undergo rapid division capable of regenerating native tissue.[53] More specifically, the connective tissue cells (including osteocytes from bone) constitute tissue growth in response to inflammation.[54] In other words, when the body sustains an injury, it is the first stage of healing—inflammation, which compels structure repair through fibroblast and chondrocyte proliferation. Extinguishing inflammation is like suppressing a fever; rather, it is best to just monitor this natural response to microbes by creating an inhospitable environment. Likewise, inflammation is best monitored and permitted to carry out its roles, including increasing circulation, and attracting the same cells that might fight bacteria or virus during a fever.

The inflammatory process is the first phase of healing, followed by proliferative and remodeling phases; if the first phase is compromised, the subsequent reactions are undermined, decreasing chances of complete tissue healing. Specifically, following injury, platelets and numerous immune cells release a potent vasodilator, histamine. This effect is prolonged by mediators such as serotonin, bradykinins and prostaglandins, which in turn encourage circulation, increase capillary permeability, allow subsequent passing of protein rich fluid to injured intercellular spaces, and attract inflammatory cells. Such complex processes lend the classic redness and warmth, swelling and pain, which characterize soft tissue injury. Often trainers and physicians are disapproving of such accompanying signals, containing them with treatments like corticosteroids and NSAIDs, but pain and swelling simply indicate properly functioning repair mechanisms. In fact, NSAIDs and corticosteroids are at best mere palliative treatments that reduce inflammation and subsequent symptoms by respectively inhibiting the enzyme cyclooxyngenase, which in turn inhibits the formation of prostaglandins, or the enzyme phospholipase A2, which blocks the production of prostaglandins and leukotrienes. Already the underlying cause of disease is neglected. Leukotrienes are hormone-like, potent chemotactic and chemokinetic agents,[55] so inhibiting these mediators jeopardizes their role of attracting immune cells to the specific area. Cortisone reduces the quantity of macrophage, or clean-up cells, inhibits fibroblast proliferation responsible for collagen production, and of course thwarts leukocytes, which stimulate the inflammatory process in the injured tissue.

Conversely, it must be noted that inflammation is unconstructive and must be subdued when it becomes systemic. This latter condition however gives inflammation an undeserved reputation. Unlike the acute state, systemic and chronic inflammation underlies the genesis of rheumatoid arthritis, life-threatening allergic reactions, cancer, and even some forms of fatal kidney disease; this notion of unmanageable inflammation has disgraced the biological response, compelling medical practitioners to stifle it in every situation. But in the case of connective tissue injuries, inflammation has chronic tendencies only if improperly handled, while the initial swelling performs an adaptive function, jumpstarting the healing process. Yes, customary treatments have their time and place, such as in complete tears, but otherwise in common tendon and ligament restoration, stimulating inflammation for faster repair is justified. And that's just what Prolotherapy does.

An alternative/complementary injection therapy firmly anchored in clinical and scientific methodology, Prolotherapy has garnered quite a following of practitioners and recipients in its 50 plus years of practice. This success is largely owed to repeated favorable outcomes in local clinical settings, as opposed to organized funding and industry sponsored research. Logically the United States Bone and Joint Decade, which strives to improve quality

of care by encouraging nonexclusive collaborative efforts, should recognize a treatment such as Prolotherapy, which meets its objective of providing low-risk, low-cost, high-quality care that could reduce direct/indirect expenditures, help speed recovery and challenge the projected statistics of impending personal and societal financial pressures. Since the initiative's launch, many advances have been made; even so, musculoskeletal conditions remain costly, chronic, and all too common to an aging population with high expectations of the health system. Accordingly, it is imperative to review and update agendas of the industry, government, hospitals and universities, which generate the majority of scientific research; that is, overcoming hurdles set up by pharmaceutically driven interests will framework the ultimate success of the Bone and Joint Decade. This involves re-educating, or rather "advancing the understanding" of government and health agencies, a very notion the Decade stresses; as a matter of course funding and research may be merited to underfunded, under-recognized unconventional treatments like Prolotherapy, which are currently criticized for unsatisfactory study designs, lack of placebo controls, and blindness. Without the fair amount of studies backing up anecdotal success, seemingly Prolotherapy is unlikely to become a mainstream Western medical therapy, after all, medical schools, which rightly adhere to grounding their education in evidence-based science, are naturally disinclined to expose students to minimally studied allopathic medical injection therapies, albeit erected on replicable and predictable clinical results, empirical data collection and of course official scientific experimentation.

THE FINANCIAL COMPONENT

As a whole, Western medicine's poor track record in treating underlying mechanical dysfunction warrants funding interventions like Prolotherapy, which if studied with blindness and controls, *ideally* may become the quality, affordable "reasonable and customary" treatments covered by health insurers today. *Realistically*, healthcare is a business not insulated from profit driven interests. According to a concept review published in *The Journal of Bone and Joint Surgery*, medicine is now an industry partly due to business principles drawn upon by government regulators; this shapes medicine, inadvertently increases overhead, encourages competitiveness and promotes struggle for market share.[56] That is quite evident when considering profit margins of customary treatments; NSAIDs are fast approaching the three billion dollar mark in annual sales,[57] with 70 to 75 million NSAID prescriptions written annually in the United States alone, with additional expenditures to treat adverse effects.[58] A retrospective cohort study examining side-effect treatment costs following NSAID administration for arthritis extrapolated that 3.9 billion was spent on treating arthritis, thus adding 45.5% to the cost of arthritis treatment.[59] As for arthroscopy, surgeons readily perform these "highly reimbursable procedures,"[60] with costs ranging in the thousands, mounted by MRI and x-ray, ancillary and rehabilitation charges.[61] Low corticosteroid costs and short treatment duration is off set by side-effect generated revenue, which as remarked upon by the *Denver Business Journal*, boosts the lucrative health care crisis[62] and the swollen bottom lines of the pharmaceutical industry,[63] which incidentally contributed more to the public record of steroid research than any other industry before.[64] A non-pharmacologic treatment like Prolotherapy on the other hand is a relatively simple procedure that uses readily available proliferant solutions like dextrose, glycerin, minerals, sodium morrhuate, autologous growth factors, and other pro-inflammatory compounds[65] that naturally offer long-term relief through stimulation of collagen formation, fibroblast production and the strengthening as well as tightening of injured connective tissue structures.

Time and again Prolotherapy delivers such results, and the basic healing mechanism is quite straightforward. A proliferant is injected, leading to local inflammation, which in turn triggers a wound-healing cascade, resulting in new collagen deposition. The naturally occurring protein shrinks as it matures, tightening and strengthening the injected ligament, tendon, meniscus, muscle, cartilage or joint of the back, ankle, wrist, hip, knee, and other such areas typically bearing the brunt of force. Because the rate of healing is rapid, and minimal injections required, Prolotherapy fell out of favor during the 1980's considering its "unprofitable" nature. After all, with Prolotherapy fewer people would require pain medication and expensive surgery, thus eclipsing the drug company foothold. Funding and advancements necessary to propel the unprofitable venture into the spotlight were thus arrested; as follows, the current volume and strength of available data is insufficient for the Medicare Board, which covers well-supported, double-blind studied therapies. But this is no longer a viable excuse for Prolotherapy's delayed success, for the societal and economic cost of musculoskeletal disease presents a compelling argument for expanding research to new fronts. Solutions lie not

in drug company sponsored research, for Prolotherapy is inherently unprofitable; after all, short treatment duration and efficient recovery targets the injury's root cause, preventing future wear and tear of supporting structures, permanently welding disabled ligaments and tendons to bone, and rendering adverse reactions near obsolete. In 1993, a survey was published, reviewing Prolotherapy injections performed by 95 physicians on a total of 494,845 patients.[66] Of these, 343,897 sought treatment for low back pain, while 98,430 for other spinal areas and 27% received non-spine peripheral joint injections. Of all the patients, only 66 reported minor complications, including 24 reports of allergic reactions and 29 cases of pneumothorax, all of which were swiftly resolved. Fourteen reports accounted major complications, which required hospitalization or ongoing care. In summary, there were only 80 complications for a total of 494,845 patients, yielding only a 0.00016% chance of complications. Literally, risks associated with Prolotherapy are continual pain relief, or rather continual pain relief following a sharp pinch when skin is punctured. In that case, patients sensitive to injections may receive local anesthesia, tranquilizers and pain medications.

One Prolotherapy study showed that for a total of 494,845 patients, only 80 experienced complications, yielding only a 0.00016% chance of complications.

Of course like any other invasive medical procedure, Prolotherapy too has potential side-effects, including risk of infection, stiffness, increased pain, bruising, bleeding, and other rarer risks. But what's more at risk is chronic pain associated with improper preliminary treatment, and at a time when joint disease accounts for half of all chronic conditions in the elderly,[67] alternative solutions are now more critical than ever. But they do not hinge on agendas of well-funded research institutes or government and health agency re-education programs; rather, solutions lie in the empowerment of the people, and their "participation in decisions about their care and treatment,"[68] as noted by the Bone and Joint Decade initiative. Forty percent of all women over the age of 50 years are expected to endure at least one osteoporotic fracture in their lifetime.[69] That is to say, 1 out of 3 women over the age of 50 are collectively encouraged to review all their treatment options and make informed decisions before settling on any therapy; with new patient expectations, physicians may be compelled to update their practices to meet demands. More than 130 million annual visits to healthcare providers rank musculoskeletal conditions as the number one reason for physician calls.[70] In other words, nearly 1 in 2 Americans over the age of 18 may be empowered to demand that research of reasonable treatments like Prolotherapy be funded, and ultimately covered by health insurers once an adequate volume of methodically conducted studies are available.

By the year 2020, elderly will account for 25% of the population in countries with developed market economies.[71] This otherwise neutral statistic alas presages an increased rate of musculoskeletal disorders that represent half of all chronic conditions in individuals 65 years and older.[72] The aging population steadily approaching the 25% demographic should take heart in the fact that Prolotherapy is available, insured or not (though hopefully so by at least 2020). Unrestricted access to this low-tech, low-risk injection procedure, at a fraction of the cost, offers a refuge for the young and elderly alike, in developed and emerging market economies, by reinforcing potential complications with tissue welding techniques, guaranteeing lasting pain relief and recovery. Prolotherapy is the solution, demonstrating in virtually every case growth of normal, stronger ligament and tendon tissue following stimulation of the body's natural healing mechanisms; and there are a sufficient amount of sound studies, including case reports, pilot, retrospective, open face prospective and double-blind placebo controlled, which confirm these facts. Dr. Y. King Liu used the knee ligament in rabbits to quantify the strength of tissue formed by Prolotherapy.[73] In his study, a 5% cold liver oil extract solution was injected 5 times into the femoral and tibial attachments of the medial collateral ligament, and then compared to non-injected ligaments. Results demonstrated significantly increased ligamentous mass, thickness, and strength. Particularly, within a 6 week period, ligament mass increased by 44%, thickness by 27% and the ligament-bone junction strength by 28%. To confirm Dr. Y King Liu's results by illustrating the tissue proliferating process, while testing how the procedure applies to tendons, Dr. J.A. Maynard and associates treated rabbit tendons with the same solution.[74] Following proliferant injections, the actual tendon circumferences increased an average of 20 to 25% after 6 weeks. The researchers observed, "The increase in

circumference appeared to be due to an increase in cell population (immune cells), water content, and ground substance (glue that holds the collagen together…) Consequently, not only is there an increase in the number of cells, but also a wider variety of cell types, fibroblasts, neutrophils, lymphocytes, plasma cells, and unidentifiable cells in the injected tissues." These findings are not unlike what biologically occurs when injured tissue self-repairs, so the source of pain and injury is mended rather than covered up, and essentially turns a chronic injury into one that is acute[75] by activating the immune system. On these grounds it is fitting to say that Prolotherapy is the solution, as it induces the natural healing mechanisms of the body by increasing circulation, in turn transferring not only nutrients but immune cells that stimulate tissue restoration through growth of collagen.

FAR REACHING EFFECTS OF PROLOTHERAPY

Prolotherapy injections are not limited to ligaments and tendons of the knee and spine, but produce similarly successful results when administered into the neck, shoulder, groin, wrists, hips, etc. Efficacy of Prolotherapy for groin functional impairments was studied in 2005 by Reeves, et al.[76] Career-altering groin/abdominal pain, non-responsive to conservative treatment trials, jeopardized top athletic performance of professional rugby and soccer players. Following monthly injections of 12.5% dextrose in 0.5% lidocaine in abdominal and adductor attachments on the pubis, 66 of 75 elite athletes returned to full elite-level, unrestricted performance in an average of 3 months. While that is impressive, osteoarthritis pain has also been studied, with successful results. In a recent double-blind placebo controlled study, knee osteoarthritis symptoms demonstrated statistically and clinically significant improvements at 1 and 3 years follow-up after injections. When present, ACL laxity improved as well.[77] In another study, finger and thumb osteoarthritis showed improvement after 6 months following Prolotherapy injections, with 42% improvement in pain and 8 degree improvement in flexibility.[78] Such findings attest to Prolotherapy effectiveness, with a healing rate averaging between 75–90%,[79] and fast recovery. The latter point is critical when considering the indirect expenditure impact on the total GDP, with prolonged recovery time comprising a major facet of productivity losses. In fact, Prolotherapy is one of the only treatments that actually encourage movement post-treatment to aid the healing process, and that itself could be considered rehabilitation. Repair and regeneration begins within the first few days and does not involve the prolonged period of residual pain and disability that, say, surgery recovery involves with the rehabilitation course potentially lasting weeks, months or even years. More over, unlike inpatient operative procedures, Prolotherapy does not require general anesthesia/epidural and the execution lasts mere minutes as opposed to hours, costing hundreds as opposed to tens of thousands, thus mitigating direct expenditures associated with customary treatments.

COST ADVANTAGES OF PROLOTHERAPY

Societal and personal financial burdens are further mitigated by the fact that Prolotherapy sidesteps expensive MRI and x-ray tests, and rejects the prolonged and costly pain medication approach, which may ultimately wear off. To put the differential costs into perspective, 2 to 3 proliferative injections for young patients and 4 to 8 for adults at approximately $250-600 per session is comparatively an inexpensive out-of-pocket medical investment; for a patient without insurance, Prolotherapy is a cost-effective, viable alternative to customary treatments like prescription pain medications that cost several hundred dollars per month, doctor recommended EMG/NCV or MRI, which may cost approximately $1,200 and $2,500 respectively, as well as pricey operative procedures, and their follow-up rehabilitation fees ranging in the hundreds per visit. Such preventable costs, which profoundly impact our nation's economy, may be arrested by redirecting focus to treatments with low administrative costs, short treatment duration and minimal risks.

As it stands, the social impact of musculoskeletal pathologies entails high costs, in terms of treatment and loss of income; a reform that aims to addresses such healthcare pitfalls must target costly treatments, which fail to deliver results and contribute to unnecessary spending. As such, reviewing the economic impact of past health spending is one of the keys to our long-term fiscal future. Total national health spending steadily increased from approximately 6% of GDP in 1965 to more than 16% in 2007,[80] and this rising health care trend, which is a major share of the economy, is expected to continue in the future.

It is projected that by 2018, national health spending is anticipated to comprise just over one-fifth, or 20.3%, of GDP.

In fact, between 2008 and 2018, average annual health spending growth is expected to surpass average annual growth in the overall economy by 2.1 percentage points per year.[81] It is thus projected that by 2018, national health spending is anticipated to comprise just over one-fifth, or 20.3%, of GDP.[82] This grave course our nation is bound for may be redirected by increasing investment in health policy research and spurring the Bone and Joint Decade initiative to revolutionize treatment approaches. That includes weeding out conventional therapies that treat distinct conditions uniformly, as well as overhauling the prevailing model of chronic pain management, which hinges on anti-inflammatory medication and injections. No matter who pays for such care, it does not offer patients better quality of life, and thereby drives up health care costs without yielding corresponding long-term benefits. Perhaps Prolotherapy doesn't after all fit in an industry whose financial incentives and insurance payment policies encourage physicians to order more tests and costly procedures, then its time to fit the industry to Prolotherapy. Besides limiting costs, this will help, not hinder physicians to fulfill their Hippocratic Oath as their tool kits are broadened to tackle complex conditions in a personalized program. Proactive physicians translates into medicine that is more participatory with a preventive focus that moves beyond adequate into optimal. (*See Table 1.*)

The benefits of Prolotherapy versus traditional methods, including surgery:

- cost effective
- safe form of long-term pain relief
- swift recovery
- general anesthesia/epidural is not required
- MRI is not required
- limits long-term medication use
- prompt return to activity encouraged/mobility not restricted
- exceptional safety track record
- minimal side-effects
- treatment is minimally invasive and quick (minutes versus hours)

Table 1. The benefits of Prolotherapy versus traditional methods.

Returning to the initial question examining whether the "reasonable and customary" treatments should be reformed to also include reasonable and *non*-customary treatments, well, that's for the patients to answer. Once patients recognize that musculoskeletal conditions, including osteoarthritis, cost nearly 128 billion per year in direct medical expenses,[83] and that Prolotherapy heals connective tissue, regardless of injury severity and location, then the answer is clear. Indeed the reform driven research trend should favor cost-effective interventions that reflect the patient's own innate regenerative capacity. National spending trends and poor results exhibited by customary treatments present compelling evidence for better coverage of therapies that may ultimately save the health industry billions of dollars per year, but more importantly save the increasing human toll by delivering care patients deserve. ■

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REMARKABLE RECOVERIES

A Hypnotherapist's Experience with Prolotherapy

Marvin "Mark" Stepp

In the spring of 2010, I severely injured my back picking up a case of books. It was not my first time to injure my back, but it was definitely the worst. Normally, when I get hurt I go to a chiropractor who gets me back up and working in three to four days. But since my worst episodes were three or four years apart, I always considered it as just part of getting older. But this last injury was different.

I started out seeing many different health care providers for my back pain, to include: a chiropractor and Chinese masseuse. I have been told that I have 5 herniated lumbar discs (one ruptured), SI joint problems, and (I found out later) my coccyx out of place.

I know pain is the main issue for most people, and it was certainly an issue for me, but I'm trained to deal with pain. I'm a clinical hypnotherapist, and helping people control their pain without drugs is part of my business. But I also know that pain is there for a reason, so I am reluctant to mask what I consider worthwhile (not chronic) pain like athletes do with steroid injections. Some of my clients had undergone steroid treatments that drastically mitigated the pain, so I investigated that first. A pain management physician, in Sugar Land, Texas, injected steroids into three of my damaged discs. He explained that the injections would not just mask the pain the way drugs did, but that the injections would reduce the swelling and allow the discs to shrink back to normal so they could heal on their own, hopefully, without having to resort to surgery. That helped a lot, but it did not relieve the pain from my SI joint and tailbone, which was radiating down my leg all the way to my foot. I was unconsciously dragging my foot so much that not only did I feel like the Igor character in a Dracula movie but, worse, I actually fell four times, twice on stairs, because my foot kept hooking on things. I was a mess.

I was referred to another chiropractor, who prescribed water therapy (exercises in a swimming pool) and massage in addition to his treatments. The water therapy was probably a lot more effective than the massage, but nothing—short of drugs or hypnosis—makes pain temporarily subside better than an expert masseuse. Also, the massage relaxed my muscles so that the chiropractor could more effectively adjust my body.

I began searching the web to look for other treatment options. Was there anything that would help me long term? Was I going to have to learn to live with pain and the lack of strength and mobility? That's when I found out about Prolotherapy.

According to the information at various websites, the rate of success of Prolotherapy (also known as sclerotherapy and proliferative injection) depends on several variables, including the patient's history and ability to heal. Up to 95% of patients suffering from low back pain with hypermobility, experience remission of pain with Prolotherapy. In comparison, the *Journal of Bone and Joint*

Mark Stepp on his motocycle and able to ride without pain after Prolotherapy.

Therapy reports a 52% improvement in patients treated surgically for disc involvement. A review of five studies involving 366 participants concluded that Prolotherapy alone was ineffective in treating chronic low-back pain. But when combined with other treatments, such as spinal manipulation and exercise, Prolotherapy can improve chronic low-back pain. Sounded good to me, especially when I found out that it supposedly helped cure SI joint problems.

I searched the web for SI joint cures and found Adam Weglein, DO, a Sports Medicine physician with the Center for Spine, Sports and Physical Medicine in Houston, Texas. He was everything I was looking for: honest, concerned, and inexpensive, which was good because my insurance does not pay for Prolotherapy. I just finished my 6th session. I'm wishing now I had gone to Dr. Weglein years ago. My pain is nearly non-existent and I'm getting my strength back.

In my own case, Prolotherapy has taken me from feeling my age to being able to do whatever I want (demonstrated by my recent 4,137-mile trip to Yellowstone on my motorcycle). I had 5 herniated discs in my lower back, plus my SI joint and tailbone were both out of place. I was in constant severe pain regardless of what position I was in. Walking, standing, and lying down hurt badly enough, but sitting was unbearable. I was walking like a 95-year-old man and could barely go to work. Other than a small twinge from the SI joint problem, I am virtually pain free today even without using my hypnotherapy techniques.

Prolotherapy, or this concept anyway, has been around in different forms since about 500 B.C. Today, the therapy requires that the doctor inject a sugar based solution, to stimulate growth factor release. In my case, he made up to 30 injections each time. Experts used to think Prolotherapy worked by inducing scar tissue in the ligaments; now they know that no scar tissue forms. It simply induces the body to shorten and heal the ligaments on its own. What a concept. ■

WONDER WHY?

Treatment of Joint Hypermobility Syndrome, Including Ehlers-Danlos Syndrome, with Hackett-Hemwall Prolotherapy

Ross A. Hauser, MD & Hilary J. Phillips

ABSTRACT

Joint hypermobility syndrome (JHS) and Ehlers-Danlos Syndrome (EDS) are both heritable disorders of connective tissue (HDCT) characterized by joint laxity and hypermobility. The conditions are both genetic disorders of collagen synthesis, where the adverse effects of tissue laxity and fragility can give rise to clinical consequences that resonate far beyond the confines of the musculoskeletal system. Both conditions have as their hallmark generalized hypermobility which can affect almost every bodily system. The hypermobility can be documented by the Brighton criteria which involves the objective measurement of the hyperextensibility of various joints. While the major presenting complaint of JHS and EDS is arthralgia in multiple joints, if the hypermobility is left unchecked, joint dislocations and degeneration may prevail.

While traditional medical treatments including education and lifestyle advice, behavior modification, physiotherapy, taping and bracing, exercise prescription, functional rehabilitation and pain medications offer some symptomatic control, they do little in regard to curbing the progressive debilitating nature of the diseases. The excessive joint mobility with its subsequent joint degeneration and multiple joint dislocations, can then lead the individual to seek out surgical intervention, which has suboptimal results in the hypermobile patient population versus the normal population. As such, some patients with JHS and EHS are seeking alternative treatments for their pain, including Prolotherapy.

Prolotherapy offers great hope for those with symptoms from generalized hypermobility because it is designed to successfully treat the ligament and tissue laxity that accompanies JHS and EDS. Prolotherapy works by initiating a brief inflammatory response, which causes a reparative cascade to generate new collagen and extra cellular matrix giving connective their strength and ability to handle strain and force. Prolotherapy has a long history of success treating ligament injuries, including patients with joint hypermobility. Studies on Prolotherapy have shown that it eliminates chronic pain even in those patients who have been told by their medical doctor(s) that surgery was the only treatment option for their pain.

Some of the rationale for using Prolotherapy for patients with EDS and JHS include that it has a high safety record, is comprehensive (all or most joints can be treated at each visit), is an outpatient procedure, is cost effective (compared to surgery), pain relief is often quick, and it provides joint stabilization. Perhaps its greatest asset is the fact that this one treatment modality can handle most of the painful musculoskeletal conditions that occur in individuals with EDS and JHS.

Prolotherapy could contribute to the treatment of hypermobility disorders also by preventing the development of precocious osteoarthritis. It has long been known that individuals with JHS and EDS suffer with premature osteoarthritis in various joints and the amount of degeneration correlates with the extent of the individuals hypermobility. The combination of extreme hypermobility and repeated injury is presumed to be what leads to the early osteoarthritis. This is most likely the reason that the hypermobility type of Ehlers-Danlos Syndrome is the most debilitating form with respect to musculoskeletal function.

While the primary author has twenty years experience treating JHS and EDS musculoskeletal symptoms with Prolotherapy, future studies will need to be conducted to best document the exact role Prolotherapy has in the treatment of the musculoskeletal symptoms and hypermobility of JHS and EDS and if it can prevent future joint degeneration in these individuals..

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KEYWORDS: Ehlers-Danlos Syndrome, hypermobility, Joint Hypermobility Syndrome (JHS), ligament laxity, Prolotherapy.

EPIDEMIOLOGY

Joint Hypermobility Syndrome (JHS) is a largely under-recognized and poorly understood multi-systemic hereditary connective tissue disorder which manifests in a variety of different clinical presentations. Also termed heritable disorder of connective tissue (HDCT), this is a heterogeneous group of genetically determined diseases, with JHS being a milder variation of Ehlers-Danlos Syndrome (EDS), where gross joint laxity often prevails. While hypermobility is a feature common to them all, they are all believed to be caused by a defect in collagen, the essential connective tissue protein responsible for tensility and integrity of skin and joints tissues.[1, 2]

While Ehlers-Danlos Syndrome is the most severe form of hypermobility, many others suffer from similar conditions such as JHS, or even benign or undiagnosed forms of hypermobility, which present many of the same characteristics as EDS. Studies have indicated that JHS affects 2%–5% of the general population, although it is estimated that 1 in 20 hypermobile patients have not been diagnosed for their disorder.[3, 4] EDS is collectively believed to affect one in every 5000 children at time of birth, although this number is a rough estimate due to the fact that EDS is widely underdiagnosed in the general population.[5, 6] At present, there are six primary known classifications of EDS: Classic, Hypermobility, Vascular, Kyphoscoliosis, Arthrochalasia, and Dermatosparaxis (*See Figure 1.*) The hypermobility type, which is found to be the most common, is estimated to affect one in every 10,000 to 15,000 individuals.[7]

ETIOLOGY AND PATHOLOGY

JHS has a strong genetic component with an autosomal dominant pattern. First-degree relatives with the disorder can be identified in as many as 50% of cases. Within this population, statistics indicate that EDS is more prevalent in those of African, Asian, and Middle Eastern descent, and affects women significantly more than men.[8-10] The syndrome appears to be due to an abnormality in collagen or in the ratio of collagen subtypes. Mutations in the fibrillin gene have also been identified in families with JHS.[11, 12]

Ehlers-Danlos Syndrome is caused by defects in the biogenesis of collagen, the major structural protein of the body. The condition can be either inherited from a parent with the defect or caused by a genetic mutation. EDS is generally inherited in an autosomal dominant pattern, though an autosomal recessive type exists. Mutations in genes encoding fibrillar collagens or collagen-modifying enzymes have been identified in most forms of EDS, including the classic and vascular subtypes. To date, the genetic background of the hypermobility type of EDS remains unclear. The exact gene involved in hypermobility type EDS is unknown, although research indicates that there may be a connection to haploinsufficiency (having less than one half of the necessary amount) of tenascin X which is encoded by the gene TNXB.[13] Family history is an important tool in diagnosing EDS, because first-degree relatives have about a fifty percent chance of inheriting the defect.[14] Unfortunately, there is no prenatal method of testing available to determine whether or not the defect has been passed down to a child.

When a defect such as the one found in EDS is present, collagen fibers become weakened, allowing tissues to become more elastic. In more severe cases, such as vascular type EDS, this can affect the tissues of the internal organs, such as the abdominal aorta, colon, and brain vessels, causing them to become weak and even rupture under pressure.[15] In the case of JHS and hypermobility type EDS, the weakened collagen fibers affect the integrity of ligaments in the joints, and ultimately the stability of the joint. The weakness of these ligaments is what allows joints to hyperextend beyond the normal physiological limits.

Figure 1. The six primary known classifications of Ehlers-Danlos Syndrome (EDS).

Classic	Hypermobility	Vascular	Kyphoscoliosis	Arthrochalasia	Dermatosparaxis
- Skin hyperelasticity - Smooth/velvety skin - Extensive atrophic scarring - Extensive bruising - Joint hypermobility	- Recurrent joint dislocation - Vertebral subluxations - Chronic joint pain	- Extensive bruising - Arterial fragility - Intestinal fragility - Uterine fragility - Tendon / muscle rupture	- Kyphoscoliosis - Arterial rupture - Atrophic scars - Excessive bruising - Osteopenia	- Congenital hip dislocation - Joint hypermobility - Recurrent joint dislocation - Tissue fragility - Kyphoscoliosis	- Severe skin fragility - Extensive bruising - Premature rupture of membranes - Hernias

Joint hypermobility, a key finding in the heritable disorders of connective tissues, is diagnostically evaluated according to the Brighton Criteria, which utilizes the Beighton Score.** Determining the Beighton score is essential for making the diagnosis of JHS because it measures generalized joint laxity. The Beighton Score measures the ability to perform certain hyperextensive functions, including significant flexion of the thumb and fifth finger, hyperextension of both knees and elbows greater than 10 degrees, and the ability to place the palms on the floor with the knees fully extended, by assigning a point to each of these functions. (*See Figure 2.*) The Brighton criteria were developed to establish diagnostic criteria for JHS. Using these criteria helps physicians to distinguish JHS from other connective tissue disorders.[16] According to the Brighton criteria, a score of four or higher on the Beighton Scale indicates generalized joint laxity and this along with athralgia in four or more joints for longer than three months signifies joint hypermobility syndrome.[17,18] (*See Figure 3.*) Typically a score of five or higher on the Beighton Scale is used as the cut-off for Ehlers-Danlos Syndrome.**

Readers should not be confused by the similarity of these two names. "Beighton" is the name of the score, and "Brighton" is the name of the criteria.

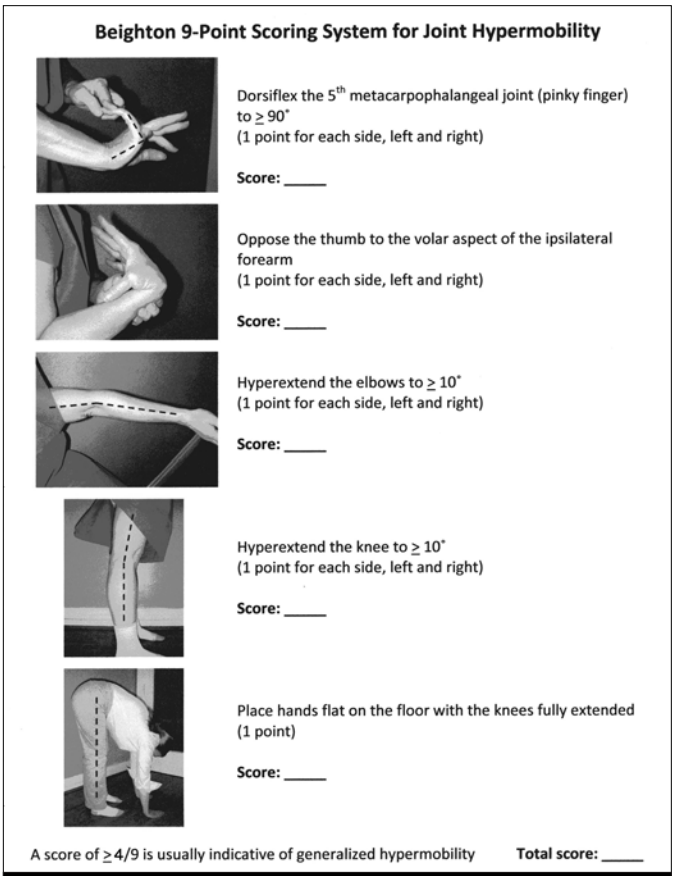

Figure 2. Beighton 9-point scoring system for joint hypermobility. A score of 4 or greater is indicative of generalized joint hypermobility.

Brighton Criteria

Major Criteria

- Beighton score of > 4
- Arthralgia for longer than 3 months in 4 or more joints

Minor Criteria

- Beighton score of 1, 2, or 3
- Arthralgia (> 3 month duration) in one to three joints or back pain (> 3 month duration) or spondylosis, spondylolysis/spondylolisthesis
- Dislocation or subluxation in more than one joint, or in one joint on more than one occasion
- Three or more soft tissue lesions (eg, epicondylitis, tenosynovitis, bursitis)
- Marfanoid habitus (tall, slim, span greater than height (> 1.03 ratio), upper segment less than lower segment (< 0.89 ratio), arachnodactyly)
- Skin striae, hyperextensibility, thin skin, or abnormal scarring
- Ocular signs: drooping eyelids, myopia, antimongoloid slant
- Varicose veins, hernia, or uterine or rectal prolapse
- Mitral valve prolapse

Requirements for Diagnosis

Any one of the following:

- Two major criteria
- One major plus two minor criteria
- Four minor criteria
- Two minor criteria and unequivocally affected first-degree relative in family history

Figure 3. Brighton Criteria for Joint Hypermobility Syndrome.

Keer R and Grahame R. *Hypermobility syndrome: recognition and management for physiotherapists.* London: Butterworth Heinemann; 2003.

** There is still some debate on the necessary criteria for making the diagnosis of Ehlers-Danlos Syndrome (EDS). While a Beighton score of 5 is indicative of EDS, a score of 4 does not preclude the diagnosis. Most agree that the diagnosis is made by a family history of the condition and the clinical evaluation. Genetic testing and muscle and skin biopsies confirm the connective tissue (collagen) disorder. Other diagnostic testing such as echocardiogram, MRIs and CT scans can be used to confirm blood vessel, valvular, and organ connective tissue problems seen in the various types of EDS.

CLINICAL PRESENTATION

While joint hypermobility is very common, occurring in 10-20% of populations of Western countries, and higher still in those in Indian, Chinese, and Middle Eastern groups, it is important to distinguish between joint hypermobility and Joint Hypermobility Syndrome.[19] People who are hypermobile without symptoms are merely people with hypermobility. Those with symptoms attributable to their hypermobility may have JHS if they conform to the Brighton criteria.

While hypermobility with arthralgias (joint pain), may sound rather benign, JHS is typically a multi-system disease that can be quite disabling. In one study out of the University of Manchester involving 125 children with JHS, 74% had arthralgia, 13% speech difficulties, 14% learning difficulties, 12% urinary tract infections 10% subluxation/dislocations of joints, while 48% had limitations of school-based physical education activities, and 67% difficulties in other physical activities.[20] Because of deconditioning, children with JHS have been found to have a significantly decreased maximal exercise capacity compared with age and gender-matched control subjects.[21] Another study linked an increased prevalence of migraine headaches with JHS.[22] It is not uncommon for patients with JHS to go 10 years or more before getting appropriately diagnosed.[23] One reason for this is doctors and others are trained to examine for reduction of joint mobility rather than for an *increased* range, so that hypermobility is commonly missed. When hypermobility *is sought* it is the most common finding among patients presenting to a rheumatologist, but more often than not, is overlooked.[24] Nearly one-half of rheumatologists are skeptical about the significant impact that JHS has on people's lives, and about three-quarters are skeptical about a significant contribution to the overall burden of rheumatic diseases.[25] Besides arthralgias, generalized joint laxity, the hallmark of the HDCTs, including JHS, is a significant risk factor for conditions such as joint dislocations, temporomandibular disorders, pathologic disc degeneration, diffuse idiopathic skeletal hyperostosis, osteoarthritis, as well as joint injury during sports.[26-30]

Typical clinical manifestations of JHS and EDS are abnormalities of the skin, joint hypermobility, recurring joint dislocations, and arthralgia. Skin abnormalities can include thin, transparent skin, significant skin hyperelasticity, easy bruising, poor wound healing, and atrophic "cigarette paper" scars. Joint symptoms, which represent some of the more severe aspects of these conditions, range widely; however, the most frequent complaints are joint pain and dislocations. Patients with JHS often say that they are "double jointed" or that they can contort their bodies into strange shapes (i.e. voluntary subluxations) or do the splits. Many JHS patients have signs and symptoms suggestive of fibromyalgia and are usually misdiagnosed.[31] These patients present with a wide variety of readily identifiable traumatic and overuse lesions, such as traction injuries at tendon or ligament insertions, chondromalacia patella, rotator cuff lesions, or back pain due to soft tissue injury or disc herniation. Others suffer the effects of joint instability, such as flat feet, recurrent dislocation or subluxation-notably of the shoulder, patella, metacarpophlangela joints, or temporomandibular joints. Others still, develop a chronic degenerative arthritis that may be a direct complication of JHS (*See Figure 4.*) For those who suffer from dislocation

Figure 4. Types of Hypermobility, by severity, using the Beighton Score.

Example: A shoulder, knee, or elbow is lax or prone to dislocation. Ligament laxity occurs in a single joint or multiple joints independent of each other. Only symptoms are hyperextension and arthralgia. **Beighton score: 1-3**	**Example:** Joint Hypermobility Syndrome Hypermobility of four or more joints occurs in the absence of any rheumatologic disease. Characterized by joint hyperextension, arthralgia, and joint dislocation or vertebral subluxation. **Beighton score: >4** **Brighton criteria:** 2 Major Criteria or 1 Major and 2 Minor Criteria, or 4 Minor Criteria	**Example:** Ehlers-Danlos Syndrome, Hypermobility Type Marfan Syndrome Osteogenesis Imperfecta Hypermobility is congenital and caused by an inheritable defect. Effects are multisystemic and can include cardiac, optical, uterine, gastrointestinal, respiratory, spinal, integumentary, and joint abnormalities. **Beigton score: >5** **Brighton criteria:** 2 Major Criteria, 1 Major and 2 Minor Criteria, or 4 Minor Criteria

of joints, the pain can be immense, and sometimes is the first indication a patient has hypermobile joints. Many hypermobile patients also experience myofascial pain, which may be explained by the extra stress placed on muscles to compensate for lax joints as the muscles attempt to stabilize the joints.

One of the more serious long-lasting affects of joint laxity is chronic joint degeneration. The increased mechanical stress caused by ligament laxity leads to chronic joint instability, making them more susceptible to soft tissue injuries. Continual instability and injury leads to an earlier onset of degenerative joint disease in hypermobile and other patients with ligament injuries than in the normal population.[32-34]

While the signs of a typical HDCT may be present, including scoliosis, pes planus, genu valgu, lordosis, patellar subluxatin or dislocation, marfanoid habitus, varicose veins, rectal or uterine prolapsed, or thin skin, often the only manifestation are hypermobile joints. Because young children are generally very flexible, the presence of a hypermobility disorder can go undiagnosed for years; joint symptoms often will not surface until adolescence as the patient becomes more active and prone to dislocation and injury.

There is an urgent need to increase the awareness of JHS and spectrum of HDCTs. These are prevalent conditions that are frequently undiagnosed and that can cause significant health problems. Beside recurrent musculoskeletal problems and signs and symptoms derived from tissue fragility, adolescents and young adults may develop osteoporosis, early osteoarthritis or dysautonomia, that are common in the disease and deteriorate quality of life. Doctors may be unaware of the prevalence of the condition, its effect on quality of life or its multisystemic nature, and may not routinely look for hypermobility in the clinical examination, especially as the condition rarely forms part of the curriculum in medical schools or in postgraduate training programs.[35-37] The erroneous view that hypermobility is a variant of normality, rather than part of an inherited connective tissue disorder is still widely held. If joint hypermobility syndrome and the other inherited connective diseases are missed on a physical examination the following problems may arise:

- Inappropriate and potentially harmful labeling or treatments may be applied on the basis of an erroneous diagnosis such as fibromyalgia, degenerative disc disease, hypochondriasis, or degenerative arthritis.
- Overzealous physical manipulation which make hypermobile joints even more lax.
- Orthopaedic operations may be done without the surgeon knowing the patient has an underlying connective tissue disorder, which may lead to poor outcomes.
- Chronic pain may lead to a potentially reversible downward spiral of immobility, deconditioning, dependency, and despair. Out of 700 patients with JHS attending the UCH Hypermobility clinic, 168 were experiencing serious pain, disability and impairment of their quality of life, some patients becoming chairbound or even bedbound.[38]

While hypermobility may be generalized or extreme in a small number of joints, it is important for pain physicians to recognize when it is present. Besides knowing the Brighton criteria, based on determination for the Beighton Score, comparing a patient's joint range of motion compared with normal ranges for age and sex can give a clinician a clue that joint hypermobility is present. There are other common clues in both children, adolescents and adults that suggest Joint Hypermobility Syndrome is present. Some of the clues that a patient has joint hypermobility include: recurrent joint dislocations, frequent ankle sprains, child with poor ball catching and handwriting skills, premature osteoarthritis, as well as laxity in other supporting tissues. (*See Figure 5.*) A small proportion of patients with generalized joint hypermobility will have one of the more serious conditions such as Ehlers-Danlos Syndrome, Marfan Syndrome or Osteogenesis Imperfecta. When these more serious conditions are considered, a referral is made to a geneticist or other clinician for genetic testing, skin biopsy or diagnostic tests, such as an echocardiogram to look for valvular defects, or other diagnostic tests on other organs to search for signs of a multisystem connective tissue disorder. It is important to differentiate JHS from the Vascular Ehlers-Danlos Syndrome, for instance, to prevent life threatening vascular hemorrhages from arterial ruptures in the latter condition.

In children and adolescents*
- Coincidental congenital dislocation of the hip
- Late walking with bottom shuffling instead of crawling
- Recurrent ankle sprains
- Poor ball catching and handwriting skills
- Tiring easily compared with peers
- So called growing pains or chronic widespread pain
- Joint dislocations

In adults
- Non-inflammatory joint or spinal pain
- Joint dislocations
- Multiple soft tissue (including sporting) injuries
- Increase in pain or progressive intensification of pain that is largely unresponsive to analgesics
- Progressive loss of mobility owing to pain or kinesiophobia (pain avoidance through movement avoidance)
- Premature osteoarthritis
- Autonomic dysfunction, such as orthostatic intolerance (dizziness or faintness) or postural tachycardia syndrome (in this form of dysautonomia, in 60˚ upright tilt the blood pressure remains constant while the pulse rate rises by a minimum of 30 beats/min)
- Functional gastrointestinal disorders (sluggish bowel, bloating, rectal evacuatory dysfunction)
- Laxity in other supporting tissues – for example, hernias, varicose veins, or uterine or rectal prolapsed

Figure 5. Common clues suggesting Joint Hypermobility Syndrome (based on observations, expert opinion, and case series).
*Ross J, et al. Joint hypermobility syndrome. *BMJ.* 2011;342:c7167.

DIFFERENTIATING EHLERS-DANLOS SYNDROME FROM JOINT HYPERMOBILITY SYNDROME

Ehlers-Danlos Syndrome should be considered in the evaluation of every hypermobile patient who has a pain complaint. A key characteristic for diagnosis and differentiation of EDS from JHS is the addition of skin findings.[39] EDS type 1 and type 2, previously known as EDS classic type, has skin that extends easily and snaps back after release. (*See Figure 6.*) The skin is fragile, as manifested by splitting of the dermis following relatively minor trauma, especially over pressure points (knees, elbows) and areas prone to trauma (shins, forehead, chin). Wound healing is delayed, and the stretching of scars after apparently successful primary wound healing is characteristic. While EDS type 4, vascular type, can have all of the above, besides easy bruising and hematoma formation in areas of trauma, the skin is translucent (visible veins on the chest).[40] These skin findings are in

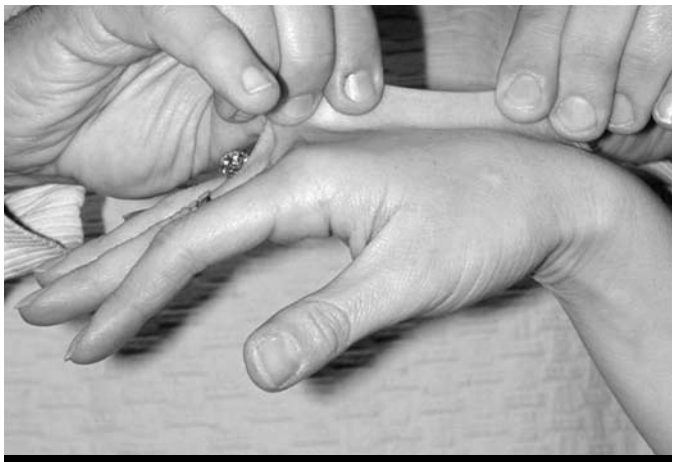

Figure 6. Patients with EDS type 1 and type 2 demonstrate skin that extends easily and snaps back after release.

contrast to EDS type 3, hypermobility type, which has soft skin with normal or only slightly increased extensibility.[41]

Skin hyperextensibility *is assessed at a site lacking excess or loose skin and without evidence of prior trauma by gently pulling until resistance is met. An ideal location is the volar surface of the forearm, where the upper limit of normal extensibility is 1-1.5 cm. Extensor surfaces of joints have excess skin and should not be used.*

All forms of EDS, like JHS, affect the joints, causing hypermobility, and as a result, individuals are more susceptible to dislocations, subluxations, sprains, strains, and sometimes fractures. While there is no distinguishing feature of the joint and neuromuscular symptoms of EDS versus JHS, EDS is often more disabling.[42, 43] The results of one study showed that 1) chronic pain in EDS is highly prevalent and associated with regular use of analgesics; 2) pain is more prevalent and more severe in the hypermobility type; 3) pain severity is correlated with hypermobility, dislocations, and previous surgery; 4) pain is correlated with low nocturnal sleep quality; and 5) pain contributes to functional impairment in daily life, independent of the level of fatigue. The authors concluded, "Therefore, treatment of pain should be a prominent aspect of symptomatic management of EDS."[44] In another comprehensive study on EDS, researchers found that over 90% suffered with chronic pain; eight was the mean number of pain locations; 70% reported continuous pain in their lower extremities, ankles, feet, toes, and hips; 89% of the pain began in childhood or adolescence; 88% were or had taken pain medications; and 51% needed narcotics. These authors concluded,

"In summary, our data reveals that individuals with EDS experience frequent and severe pain through much of their lives."[45] The severe crippling pain of EDS often prevents patients from participating in sports and having a lower quality of life.[46] Other authors have confirmed the widespread pain symptoms of the condition with the hypermobility type of EDS to be the most debilitating form, with respect to musculoskeletal function, especially affecting ambulatory ability.[47, 48]

TRADITIONAL TREATMENTS

Management of JHS and EDS frequently includes education and lifestyle advice, behavior modification, manual therapy, taping and bracing, electrotherapy, exercise prescription, functional rehabilitation and collaborative working with a range of medical, health and fitness professionals.[49] Progress is often slow and hampered by physical and emotional setbacks. The functional rehabilitation process is frequently lengthy, with education of the patient and family, sensitively prescribed and monitored physical therapy interventions and facilitation of lifestyle and behavior modifications being the mainstay of the plan.[50] Sometimes with a carefully considered management strategy, amelioration of symptoms and independent functional fitness can sometimes be achieved. Currently, there are no randomized controlled studies regarding the effects of existing treatments.[51]

At present, there is no cure for collagen and connective tissue deficiencies of Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome. The musculoskeletal symptoms derive from a vulnerability to injury resulting from fragile collagenous tissues (tendon, ligament, muscle, bone, cartilage, menisci, labrum, and skin). Conservative treatments such as physiotherapy can help hypermobile patients by the use of mobilizing techniques to restore subluxations; enhance general fitness to offset or reverse the tendency for the body to lose condition by lack of exercise; core and joint stabilizing and proprioception enhancing exercises to decrease pain and prevent further injuries.[52] As joint complaints increase with vigorous and repetitive activities, patients with JHS and EDS learn that overtraining and exercises that focus on joint flexibility rather than stabilization increase joint pain and risk of injury, thus, they need to be curbed.[53, 54] Patients refrain from activities that cause joints to lock or overextend. If avoidance of these activities is not an acceptable option for patients, physicians often try other approaches including chiropractic or osteopathic manipulation. While these approaches can give some symptomatic relief they offer little as far as long term solutions.[55, 56]

Pain management is a critical element in the treatment of hypermobility. While physical therapy and exercise may lend some degree of pain relief, individuals with hypermobility often require additional measures to manage joint pain. Patients with hypermobility disorders are often prescribed large doses of pain medication, such as acetaminophen, muscle relaxants, NSAIDs, and antidepressants; over time, stronger medications (including narcotics) and higher doses may be required to deal with the effects of chronic pain. These medications are helpful in management of symptoms that prohibit patients from carrying out certain activities, but they have no effect in treating the underlying pathology of hypermobility, and in some cases they may actually have a negative effect on joint tissues. Non-steroidal anti-inflammatory drugs (NSAIDs) are one class of medications commonly prescribed for joint pain, but can have a combative effect on joint health, due to their role in inhibiting the synthesis of collagen and articular cartilage synthesis.[57] This can cause not only weakness in ligaments, but also in cartilage, tendon, and bone cells, contributing to an overall weakening of the joint.[58, 59]

Another approach used to help with the painful symptoms of hypermobility is splinting and bracing to try to stabilize the joints. This, along with proper physical and occupational therapy to help strengthen muscles and to educate people how to properly use and preserve joints is helpful, but limited. In general, traditional medical intervention is limited to symptomatic therapy. When the symptoms continue to progress and/or are of an emergent or severe nature then surgical intervention is called upon.

Many individuals will have undergone several orthopedic procedures, even prior to diagnosis. It is quite common for the average patient with EDS, or those severely affected with JHS, to undergo multiple musculoskeletal surgeries throughout their lifetime to combat joint injury degeneration and dislocations from hypermobility.[60] Common operations include tendon transplant or transfer, capsulorraphy, arthroscopic surgery and arthroplasty.[61, 62] The degree of stabilization and pain reduction, overall patient satisfaction, and duration of improvement are quite variable. Unfortunately, the

Tendon transplant *– relocation of a whole tendon whereas a tendon transfer is the relocation of the tendinous insertion only to stabilize or improve function of a joint.*
Capsulorraphy *– suture of a tear in a capsule, especially of a joint capsule to prevent recurring dislocation.*
Arthroscopy *– examination of a joint, specifically, the inside structures and then repair or remove damaged structures.*
Arthroplasty *– surgery to relieve pain and restore range of motion by realigning or reconstructing a joint.*

weakness of hyperelastic joint tissue presents a poor healing prognosis, and surgery has proven to be widely unsuccessful in the hypermobile population.[63, 64] Grahame and Keer explain that this is because hyperelastic tissues are "less robust and amenable to surgical procedures" than healthy joint tissues.[65] When surgery is performed, the patient and physician should cautiously anticipate some improvement but expect less than optimal results.[66] While such surgical measures may provide temporary pain relief and stabilize the joint for a short time, using the surgical treatment model for cases of severe generalized hypermobility poses a problem on account of the following:

- The underlying systemic connective tissue deficiency makes surgical outcomes less predictable.
- The condition is systemic and involves multiple joints and body tissues.
- The amount of surgical procedures can be unending because of the systemic nature of the conditions.
- Each subsequent surgical procedure on any given tissue or joint is less successful.

The lack of long-lasting relief in any of these traditional treatments provides a grim prognosis for anyone living with the chronic disabling pain of Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome. The common flaw in each of these traditional treatments is their inability to repair the weakened connective tissues causing the hypermobility. Logically, then the best approach would be the one that directly addresses the root of the disability, weakened connective tissues, such as ligaments and joint capsules, by inducing their repair to stabilize the affected joints.

PROLOTHERAPY

Because surgery carries risks and complications and often does not cure pain symptoms in patients with JHS and EDS, patients are seeking alternatives with the same or greater results. Prolotherapy is one alternative that patients are turning to. Prolotherapy works by initiating a brief inflammatory response, which causes a reparative cascade to generate new collagen and extra cellular matrix giving connective tissue their strength and ability to handle strain and force.[67, 68] High-resolution ultrasounds and MRIs have been used to confirm that Prolotherapy does indeed stimulate tissue growth.[69, 70] One double-blinded animal study by Dr. Liu showed that Prolotherapy increased ligament mass by 44%, ligament thickness by 27%, and ligament bone junction structure by 28%.[71] A human double-blinded study showed joint stabilization by Prolotherapy correlated with patient outcome improvement.[72]

The doctor that introduced Prolotherapy into mainstream medical practice was George S. Hackett, MD, who described it as follows, "The treatment consists of the injection of a solution within the relaxed ligament and tendon which will stimulate the production of new fibrous tissue and bone cells that will strengthen the weld of fibrous tissue and bone to stabilize the articulation (where the bone and ligament meet) and permanently eliminate the disability."[73] He published his results in peer-reviewed, mainstream medical journals and wrote a book summarizing his results and the technique entitled *Ligament and Tendon Relaxation Treatment by Prolotherapy*.[74-76] He showed via animal studies that Prolotherapy induced the proliferation of new ligament tissue that had the effect of stabilizing joints, thereby eliminating the disability associated with ligament laxity.[77-79]

Prolotherapy has a long history of success treating ligament injuries, including patients with joint hypermobility.[80, 81] Studies on Prolotherapy have shown that it eliminates chronic pain even in those patients who have been told by their medical doctor(s) that surgery was the only treatment option for their pain.[82-85] Some of the rationale for using Prolotherapy for patients with EDS and JHS are that it has a high safety record, is comprehensive (all or most joints can be treated at each visit), is an outpatient procedure, is cost effective (compared to surgery), pain relief is often quick, and it provides joint stabilization. Perhaps its greatest asset is the fact that this one treatment

List of Musculoskeletal Conditions

Arthralgia	Ligament laxity
Barré-Lieou syndrome	Ligament sprain
Cervical instability	Meniscus tears
Chondromalacia patella	Myofascial pain syndrome
Chronic muscular pain	Post-surgical pain
Degenerative disc disease	Osteoarthritis
Degenerative joint disease	Pain after joint dislocations
Flat feet	Recurrent joint sprains
Headaches	Rotator cuff syndrome
Joint hypermobility	Scoliosis
Joint instability	Soft tissue rheumatism
Joint laxity	Spondylolisthesis
Joint subluxations	Spondylosis
Joint swelling	Tendon strains
Labral tears	TMJ syndrome

Figure 7. Painful musculoskeletal conditions that can occur in EDS and JHS which may be effectively treated with Prolotherapy.

modality can handle most of the painful musculoskeletal conditions that occur in individuals with EDS and JHS. (*See Figure 7.*)

Prolotherapy could also contribute to the treatment of hypermobility disorders by preventing the development of precocious osteoarthritis. It has long been known that individuals with JHS and EDS suffer with premature osteoarthritis in various joints and the amount of degeneration correlates with the extent of the individuals hypermobility.[86-88] Dr. P. Brighton who developed the criteria to determine joint hypermobility (for whom the Brighton criteria is named) found that when individuals had Ehlers-Danlos Syndrome and a Beighton score of at least 4, 100% of them developed osteoarthritis by the age of 40.[88] The combination of extreme hypermobility and repeated injury is presumed to be what leads to the early osteoarthritis. This is most likely the reason that the hypermobility type of Ehlers-Danlos Syndrome is the most debilitating form with respect to musculoskeletal function.[89]

TWENTY YEARS EXPERIENCE TREATING JOINT HYPERMOBILITY SYNDROME AND EHLERS-DANLOS SYNDROME WITH PROLOTHERAPY

I (R.H.) joined the practice Gustav A. Hemwall, MD in 1993, at which time Dr. Hemwall had already been performing Prolotherapy for nearly 40 years after learning the technique from Dr. George Hackett at his office in Canton, Ohio in the mid 1950s. I can remember the point Dr. Hemwall made to me in April of 1992, while first observing in his office. He said, "Most chronic pain is from ligament laxity." When I finished my first draft of *Prolo Your Pain Away!* there was a small section on both benign congenital hypermobility (also termed Joint Hypermobility Syndrome) and Ehlers-Danlos Syndrome. The reason for including them was obvious. Prolotherapy caused a significant improvement in the quality of life of individuals who had a genetic connective tissue disorder causing systemic hypermobility, the very condition (though extreme) for which Hackett-Hemwall Prolotherapy was designed to treat. One patient in those early years of working with Dr. Hemwall comes to mind.

JM was a young woman in her 30's, who had the hypermobility type of EDS, and was already confined to a wheelchair when she originally consulted with Dr. Hemwall. By the time I first saw her, she was walking, running and leading a normal and fulfilling life. Initially, she required intensive Prolotherapy for about 18 months, then twice a year for a couple of years. But after that time she was done with treatment. Prolotherapy had stabilized the joints enough, to where now it has been over 10 years since she required treatment. The intensive Prolotherapy involved treating most of the joints in her body, and she was treated over the course of two days each time. The first day, she would receive treatment to half of her joints, and the second day the other half would be treated. This is an extreme case, but mentioned to show the extent of the possibilities with Prolotherapy.

REPRESENTATIVE CASE HISTORY

JD presented to Caring Medical with a long history of severe joint pain and complaints of frequent dislocations of both elbows, knees, and shoulders, as well as subluxations throughout the spine and the sacroiliac (SI) joints. She had first begun experiencing joint pain at the age of ten, and her symptoms escalated during her teen years as she became an avid track and field athlete. The first incident of joint dislocation occurred when her knee completely gave out during a track meet. Following this event, JD underwent multiple knee reconstructive surgeries which provided short term relief, but she continued to experience pain and instability in that knee. At the age of 21, JD began experiencing cardiovascular symptoms including tachycardia and feeling faint. When she consulted a cardiologist, JD learned that she suffered from Ehlers-Danlos Syndrome.

Over the course of her adult years, JD's condition began to affect other joints in her body including her shoulders, elbows, and sacroiliac joint. Simple activities such as walking, or even a strong wind, JD said, could cause her joints to dislocate on a daily basis. In addition to being unable to walk, she was unable to use crutches or a cane because these would cause dislocation in her shoulders and elbows. Like many others who suffer from Ehlers-Danlos Syndrome, JD's condition had impeded her education and prohibited her from being able to work for extended periods at a time. When she came to Caring Medical for evaluation, JD had already undergone eight unsuccessful musculoskeletal surgeries and years of physical therapy, with no lasting improvement. Unless she found an effective treatment for her condition, she would be disabled for the rest of her life. Her initial questions were simple: Could Prolotherapy prevent the multiple joint dislocations that were occurring on a weekly basis? Could Prolotherapy give her enough pain relief so she would not be disabled the rest of her life and be strong enough to find work and support herself? The answer, based on my experience (R.H.) with treating Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome to both questions is a solid "yes." However, it should be noted that if an individual with JHS or EDS is treated early in the disease course, where hypermobility is their primary problem, the extent of the Hackett-Hemwall Prolotherapy needed will be much less than after the person has suffered from multiple dislocations and several reconstructive joint surgeries.

CASE STUDIES

Caring Medical is a comprehensive Prolotherapy practice. In the years 2009-2010, 102 patients were seen, with 85 being women and 17 being men, who carried the diagnosis of Ehlers-Danlos Syndrome or Joint Hypermobility Syndrome. This represented approximately 8% of the total patients seen during this time. The following cases are typical of the response one would expect utilizing Prolotherapy in the treatment of JHS or EDS, where resolution of the individual's joint instability/hypermobility is the primary concern.

CASE STUDY: 21 YEAR-OLD FEMALE WITH EHLERS-DANLOS SYNDROME, HYPERMOBILITY TYPE

EK first began experiencing the symptoms of Ehlers-Danlos Syndrome, Hypermobility type in the fifth grade, when one of her knees subluxed. Over the next 12 years, the pain and joint subluxations spread to other joints including the other knee, elbows, shoulders, and spine. EK tried many different forms of therapy including physical therapy, massage, ultrasound, taping, and compression braces which managed her pain well enough to perform daily activities as well as gymnastics, track, and cross country. At the age of 19, she tore the meniscus in her right knee and underwent surgical meniscus repair. Following the operation, she experienced intense pain, and subsequently underwent a second operation. While the symptoms in her knee appeared to be resolved, pain in her other joints persisted. During this time, EK also began experiencing other health issues including hypothyroidism, eczema, chest pains, food allergies, irregular menstrual periods, and degenerative disc pain in her neck and back.

In the search for a treatment for her joint pain, EK found Prolotherapy, which she felt was needed for the pain in her neck, thoracic, low back, knees, and shoulders. During this time, she continued physical therapy, and managed her pain with multiple medications. After a year and a half of minimal improvement, her pain doctor referred her to Caring Medical in Oak Park, Illinois for Prolotherapy. As a 21 year-old college student, EK was living with constant joint pain, which disturbed her ability to exercise, study, and sleep. She contemplated dropping out of school. By this time, she also suffered from joint dislocations in her shoulders and elbows causing its own amount of excessive pain and stiffness. Her spine, including the neck, thoracic, and lumbar regions, would also "freeze," sending shooting pain up and down her back.

EK's first Prolotherapy treatment at Caring Medical consisted of Prolotherapy injections to her neck, spine, both scapulas, low back, and knee. Within a week of her first visit, EK reported a decrease in her thoracic and scapular pain and improved physical stamina and energy. A month later, she began running again and no longer required treatment to her knee. By her second visit, EK had discontinued all use of pain patches, and only required occasional Tylenol for pain and muscle relaxers to help her sleep. For the next six months, EK continued to receive monthly treatments to her neck, thoracic, and shoulders, showing gradual improvement of pain and well-being. After eight months of treatments, EK no longer required any pain medications, was no longer experiencing any joint dislocations, and was back to running and gymnastics. After her initial eight months of therapy, she was seen an average of once per

year throughout her college and Masters program. She has not been seen for treatment for over seven years now, during which time she has received a PhD in her chosen profession. She continues to lead a full life, without daily pain or disability. She has no limitations while exercising most days.

DISCUSSION:

Sometimes Prolotherapy is so successful that when the joints are stabilized, even clients with Ehlers-Danlos Syndrome, do not need further treatments. To be fair, EK did need more than the customary three to six visits, most likely because of the Ehlers-Danlos Syndrome. I have not seen this client for over seven years, but have communicated with her, and I can emphatically say that she now has a completely normal productive life. She went from living in fear of multiple subluxations in multiple joints, to complete stability in those joints, even with exercising most days. Prolotherapy, in this patient with Ehlers-Danlos Syndrome, appears to have permanently stabilized the unstable joints. The next case is presented because some patients with Ehlers-Danlos Syndrome, Hypermobility type, need periodic care to keep the various joints from dislocating or subluxing.

CASE STUDY: FEMALE WITH EHLERS-DANLOS SYNDROME, HYPERMOBILITY TYPE

PF is now a 55 year-old retired school teacher and mother of two adult children who lives in Canada. She came to Caring Medical because her Prolotherapy doctor, Fred Cenaiko, MD, retired. She had always known she was "hyperflexible" but had controlled her various joint aches, pains, and subluxations with physiotherapy and chiropractic care. Her pain became unbearable 15 years prior to the first visit at Caring Medical, when she began experiencing pain and instability in her left sacroiliac (SI) joint. After seeing many specialists over the course of several months for her SI pain, including her general practitioner, orthopedists, physiotherapists, and chiropractors, PF was left upset and disappointed by her continued pain and lack of improvement. She was having difficulty working, in addition to raising her two children. If something wasn't found to help the unrelenting pain, she was destined to soon be completely disabled. Chiropractic adjustments helped for a few hours only to have her lower back go out again. She was told by one orthopedist to get a sacroiliac fusion.

As her low back pain increased, so did the rest of her joint pain. Her popping, clicking, and a feeling of looseness throughout her body increased. No longer were physiotherapy and chiropractic manipulation able to control her pain. Within a year, she had whole body pain and instability that almost completely disabled her for two and a half years. She was unable to take care of her children and she had to rely on strong pain medications in order to function. One day, her European-trained physiotherapist gave her some research articles from medical journals that talked about the tightening of joints with Prolotherapy. PF noted that the main doctor doing Prolotherapy was in Oak Park, Illinois, Dr. Gustav Hemwall. When she called Dr. Hemwall's office, she was referred to Dr. Fred Cenaiko who worked in Saskatchewan, Canada. It was Dr. Cenaiko who diagnosed PF with Ehlers-Danlos Syndrome, Hypermobility type, and began treating her back and other areas of her body every six weeks with Hackett-Hemwall dextrose Prolotherapy. It took PF, 1.5 years of receiving dextrose Prolotherapy to her lower back to experience complete resolution of her SI pain. She reports that her other joints, including her knees, shoulders and hips healed much more quickly and she only required a couple treatments to each joint to resolve her pain complaints.

After one and a half years of doing Prolotherapy, PF was completely pain free. Because various joints of her body would begin to sublux and become painful over time again, she and Dr. Cenaiko realized that receiving Prolotherapy two to three times a year was what was needed to keep her stable and pain-free. PF has continued to receive Prolotherapy two to three times per year for the past 13 years. She was able to complete the necessary years as a teacher to be eligible for full retirement benefits from teaching. Prolotherapy also helped her get back to being the type of mother, wife, and friend that she wanted to be. PF currently swims laps, jogs, or hikes on a daily basis with no pain. She states that she also enjoys biking but she has to be careful because if she cycles at a high resistance for long distances, her knees start to become unstable. PF also avoids massages because she has noticed that massages tend to loosen her joints. Dr. Cenaiko retired in 2010 and referred PF to Caring Medical to continue her maintenance Prolotherapy treatments.

DISCUSSION:

It has not been the "norm" at Caring Medical for a client with Ehlers-Danlos Syndrome to need periodic Prolotherapy treatments. Dr. Cenaiko used dextrose as the proliferant for PF. When I evaluated her and noticed that indeed there were some joints that were unstable, I suggested at her first visit to Caring Medical that we use a strong proliferant. To start, she received dextrose Prolotherapy with sodium morrhuate added to the solution. While she still believes she will need Prolotherapy twice per year, it is my hope that we will get her joints stable enough with the stronger Prolotherapy treatments, that eventually she will no longer need Prolotherapy.

This case is presented here so patients with Ehlers-Danlos Syndrome know that generally Prolotherapy can permanently stabilize joints. But some patients, like PF, are happy that Prolotherapy is available if periodic treatments are necessary.

CASE STUDY: 31 YEAR-OLD FEMALE WITH JHS, WITH CONSTANT SHOULDER, THORACIC AND RIB SUBLUXATIONS

NP is a 31 year-old registered dietitian who came to Caring Medical in February 2009 from a referral by her osteopathic doctor, because of the diminishing benefits manipulation was having on her pain. She was very interested in the potential benefits Prolotherapy might have on her significant shoulder and thoracic/rib pain. She stated that she "has always had loose joints" and for most of her adult life has needed either chiropractic or osteopathic care to function. Her significant pain started 10 years earlier while on the rowing team at college. Her primary pain was located in the left T1-T4 area and left shoulder. A previous MRI of the thoracic area was read as normal. She had tried acupuncture, electrical stimulation, physical therapy, and various medications and manual therapies without lasting relief.

On physical examination, she had noticeable ligament laxity in multiple thoracic/rib junctions (costovertebral) and her left shoulder easily subluxed anteriorly. Her Beighton Hypermobility Score was 5. At the initial visit, dextrose Prolotherapy was given to her left thoracic facets and costovertebral junctions. When seen one month later, she felt 40% better and another Prolotherapy treatment was given to the same area. She was not seen again until June and felt her thoracic pain didn't need treatment anymore but she wanted to start treatment for her left shoulder instability. Because of the degree of instability, sodium morrhuate (1cc/10cc syringe) was added to the dextrose Prolotherapy solution and treatment was given primarily to the anterior shoulder.

NP did not return for one year because of resolution of her thoracic and shoulder pain with the previous Prolotherapy treatments. When seen in June 2010, her primarily complaints were clicking, pain and an "unstable feeling" in the left hip. On physical exam, a definite palpable click was felt and a moderate degree of instability was seen. Her anterior and posterior left hip was treated on that date and again one month later. She had complete resolution of these symptoms. She was seen in October 2010 because of low back pain which wasn't resolving with physical therapy and exercises. Physical examination revealed hypermobility of her left sacroiliac joint. Dextrose Prolotherapy with sodium morrhuate was administered to the left lower back region emphasizing treatment of the left sacroiliac joint.

When NP was seen again in February 2011, the only complaint she had was recurring subluxation of her left shoulder joint during activity. She again had evidence of shoulder joint instability anteriorly. Treatment of dextrose Prolotherapy with sodium morrhuate to this area resolved this issue.

DISCUSSION:

It is common with genetic hypermobility cases for symptoms to "pop" up in other joints once the primary painful and hypermobile areas are stabilized with Prolotherapy. For instance, NP had hip instability that was stabilized with Prolotherapy, subsequently causing her hypermobile left sacroiliac joint to cause symptoms. The nice effect of Prolotherapy is that even with genetic hypermobility syndromes, the joint pain is often relieved permanently. But sometimes periodic treatments are needed because of the recurrence of joint hypermobility in a previously treated area.

CASE STUDY: 22 YEAR-OLD COLLEGE STUDENT, SELF-MANIPULATOR WITH SEVERE BILATERAL SHOULDER AND KNEE PAIN AND INSTABILITY

JR, a 22 year-old male college student, came to Caring Medical in April of 2010 for complaints of bilateral knee swelling and shoulder instability. His lateral knee swelling

began after he took up running in 2009 in preparation for entering the military upon graduation from college. He stopped running and was evaluated by an orthopedic surgeon who did an MRI and found an oblique tear of his lateral meniscus in both knees. The surgeon recommended arthroscopic surgery but JR looked for an alternative. He received one platelet rich plasma (PRP) injection on three separate visits with only minimal help. He sought a consultation at Caring Medical for Prolotherapy because of the minimal improvement with the PRP injections alone.

His shoulder issues started in 2005 (at age 17) after he tore the labrum in his right shoulder and had surgery to repair the tear. Despite having surgery, he continued to feel instability and pain in his shoulder. Because of his bilateral knee and shoulder pain and instability, even his ability to do non-impact sports like swimming had been affected.

Physical examination revealed joint hypermobility throughout his body, with a Beighton Hypermobility Score of 5. JR admitted that he frequently self adjusts or pops many of the joints in his body. Physical examination of his knees revealed significant bilateral grinding/crepitation with moderate to severe patellar hypermobility. He was instructed not to self manipulate his joints upon starting Prolotherapy, as this could potentially disrupt the connective tissues that are repairing after treatment. Dextrose Prolotherapy with sodium morrhuate was administered around the patella, as well as the various ligaments of both knees. Bilateral intraarticular Human Growth Hormone (2iu/joint) was also given. Because of the improvement in his knee pain with the first treatment, when seen one month later, his shoulders were also treated. He did not return until five months later, because of some continued symptoms, though he was feeling more stability and strength in his knees and shoulders. The knees were no longer swelling and he was back to an active exercise program.

JR returned for three more treatments from October to December 2010. This totaled five treatments to his knees and three treatments to his shoulders. At his last visit, JR reported that he was back to swimming and weight training without limitation, and only had an occasional crepitation in his shoulders but did not have pain. As for his knees, the crepitation was greatly decreased as well as the swelling. He has not yet tested his knees by running.

DISCUSSION:

This case shows that some folks, even with Joint Hypermobility Syndrome, may be doing something to themselves to worsen his or her condition. In this case, JR was what we term a "self-manipulator." He was manipulating himself an estimated hundred times per day. It becomes a habit. He cracks his neck, low back, thoracic, shoulders and other joints. It is imperative for hypermobile patients not to self-manipulate as this just further stretches the ligaments and makes them even more hypermobile. Eventually they are so loose that the only way they can keep in place to is to self manipulate. Obviously, Prolotherapy to the joint and spine instabilities is a better option. In JR's case, I (R.H.) believe he should get treated until he is back to running.

CASE STUDY: 18 YEAR-OLD FEMALE GOES FROM ANTI-DEPRESSANTS AND ANTI-ANXIETY MEDICATIONS TO PAIN FREE AT 28

When SB came to Caring Medical in March 2009, you would not have believed that this was the same woman who had walked into the office in 2001 as an 18 year-old. She was now a graduate of the prestigious Chicago Art Institute, happily married, and able to exercise. She was taking no medications. This was a far cry to the person seen in 2001 who was in constant pain and on Zoloft, Tylenol #3, Prozac, Clonazepam, Effexor and Soma. From the age of six to 12, SB was active in gymnastics. She had to stop gymnastics when her right hip became painful and, despite lots of therapies and doctors, developed into a constant throbbing pain. Her list of previous therapies to resolve this pain included: physical therapy, prescription medications, deep tissue massage, nerve blocks, acupuncture and Feldenkrais. At the time of her initial consult, she was almost suicidal because the pain was so bad. On physical examination, she had joint hypermobility throughout her body, with a Beighton Hypermobility Score of 6. After a thorough discussion that her prognosis was good but would require a lot of Prolotherapy, she and her mother agreed that SB should start Prolotherapy on her right hip, which was diagnosed as hip joint instability with labral tear.

SB came in somewhat regularly for a two year period, during which time she received dextrose Prolotherapy with sodium morrhuate. She was slowly weaned off of all of her medications. By the time was she was 20, her hip was stable and pain free. She was back to regular exercise

and attending college. From the years 2002-2007 she was seen once to twice per year because of joint instability in other areas including the shoulder, neck and elbow. The reason she came to the office in March 2009 was for what she called "tune up treatments" of her right hip and shoulder, at which time she wrote she was forever grateful for Dr. Hauser and the Prolotherapy treatments. She was seen once in 2010 for the same "tune-up treatments." She noted that the Prolotherapy had gotten her 95% better, but could feel the right hip and neck symptoms recurring.

DISCUSSION:

It is important to note for patients with JHS and EDS that, in some instances, Prolotherapy can give permanent relief to an unstable joint. Sometimes, perhaps because of the genetic component to the conditions, patients with JHS and EDS may need what SB calls "tune-up" treatments once or twice a year. While this is not ideal, the patients typically don't complain because the rest of their lives are extremely "normal." Even if a joint becomes too unstable, they have the knowledge that Prolotherapy can always be used. There is comfort in this fact. SB has not taken pain medications, except an occasional acetaminophen, in years. She has been off anti-depressants and anti-anxiety medications for over eight years, and has not seen a psychiatrist in over 10 years. She is one of the most delightful people I have ever had the opportunity to meet and treat.

CASE STUDY: ACTIVE 61 YEAR-OLD FEMALE WITH JHS

In January 2009, BB, a 61 year-old skier, came to Caring Medical saying she "didn't want anything to slow her down." BB always knew she had a tremendous amount of joint flexibility, and thus, excelled at yoga as well.

She had a significant past medical history with five years of suffering with bilateral hip, knee, and elbow pain. She continued to be active, including skiing with a very restrictive knee brace, despite her right knee MRI showing a medial meniscus tear, and her right hip MRI showing a high-grade partial-thickness tear involving the gluteus minimus insertion onto the right greater trochanter as the dominant finding with paritendonitis and trochanteric bursitis; low-grade tenoosseous strain of the iliopsoas insertion the lesser trochanter without tendon tear; more substantive iliopsoas bursitis. BB was a strong natural medicine advocate and exclaimed that "No orthopedic surgeon is doing surgery on me!" She was told by a skiing friend to look into Prolotherapy.

BB was diagnosed with JHS and like SB, had evidence of hypermobility throughout. Her Beighton Hypermobility Score was only 4, but many joints had excessive mobility. She was told that she was an excellent Prolotherapy candidate, but because so many joints were involved it would require some time for all of the instability to resolve.

BB was seen at Caring Medical on 10 occasions over the course of the next two years for treatment. Her elbow responded after four treatments, allowing her to get back to exercise, which included weights and push-ups. Her right knee needed five treatments, and her hips each needed nine treatments. Now BB is back to cycling up and down the hills of Colorado and skiing at a high level without braces and without pain.

DISCUSSION:

Some patients with JHS and EDS can function at a high level for most of their lives without needing a lot of medical intervention. In BB's case, her body didn't start to suffer the effects of her hypermobility until she was in her mid 50's. She is an extremely motivated and active person who tried everything she knew to stabilize her joints. When the orthopedic surgeons in Colorado started talking about various "potential" surgeries for her, she looked into Prolotherapy. I suspect that with her extreme sports mentality I may be seeing her periodically for a while. But I am happy for her being able to get back to all of her activities without braces, and look forward to her having an extremely "active" retirement!

CASE STUDY: 48 YEAR-OLD NATIONAL CALIBER ATHLETE WITH PELVIC FLOOR DYSFUNCTION AND JHS

JD came to Caring Medical in extreme distress because she was no longer able to work as a physiotherapist, athletic trainer and Pilates instructor. She was a 48 year-old wife and mother from Ontario, Canada and her pelvic pain had completely disabled her. She explained that her previous life as an athlete included Canadian National rhythmic gymnastics team, international level dragon boat and outrigger paddling, recreational triathlons, cross country skiing and water skiing.

JD always had what she called "extreme flexibility." She had a series of injuries including the following:

- 2004 – plantar fascia pain
- 2006 – severe hip pain on the greater trochanter
- 2007 – inguinal pain, requiring inguinal hernia repair x 2
- 2008 – right groin exploratory surgery and inguinal nerve ablation. Her right groin pain did not resolve. MRIs at this time revealed a torn rectus abdominus, right hip dysplasia, and labrum tear.
- 2009 – right rectus abdominus repair and removal of mesh. Re-injury of right inguinal area. Another right inguinal hernia repair with mesh.

JD's first appointment at Caring Medical was in August 2009. She had multiple complaints but her primary pain areas were the pelvic floor, pubis, groin, left knee and left ankle. She received some Prolotherapy in Canada previously, but because she did not feel the technique used was aggressive enough, she was not happy with the results. JD said her main goal was get to back to teaching Pilates full time. The pain was completely disabling her from working and driving, and she was becoming very depressed. Her pain was increased with most movements and activities including sitting, standing and walking. She was diagnosed with JHS with her main problem being subluxation of the pubic symphysis. She was felt to have pubic instability and this was causing the majority of her pelvic pain. She had instability of the left knee and left ankle. These areas were treated with dextrose Prolotherapy with sodium morrhuate every four to six weeks. When JD came for her third visit in December 2009 she noted that she was feeling much better. Her groin pain had improved to the point that she was water jogging two to three times per week and doing some core workouts. She started working again, two mornings per week, and was able to drive short distances. On this third visit, she started treatment on her right hip because of popping, clicking and pain from hip joint instability. She was feeling much stronger and less pain overall until she re-injured her right oblique abdominal muscle and this started her right pubic/groin pain again.

At her February 2010 visit, the pubic symphysis was treated again, as well as the right hip. At this visit, JD noted a new pain in her lower right back which was also treated with dextrose Prolotherapy with sodium morrhuate at that time. Over the course of the next year, JD was seen in the office three times (including seven months between two of the visits) necessitating treatment to her left knee, right hip, and new-onset metatarsalgia of her left foot. To date, her disabling groin pain is down to a manageable level, but feels that some of the pain is secondary to the two meshes she has in her. JD is back to work, but not full time like we had hoped.

DISCUSSION:

When writing case studies, it is often difficult to illustrate the extreme disabling effects of JHS and EDS. I included the case of JD to show that a national caliber athlete can be broken down by these conditions to the point where she could not even work as a full-time athletic trainer/ Pilates instructor. In her case, she was on the verge of a nervous breakdown prior to Prolotherapy, and shed many tears at her first consultation. When she was most recently seen, in February 2011, it was primarily because she had fallen on the ice and re-aggravated her right hip and left knee pain. Her groin was not treated, which was the original disabling injury for which she first came to Caring Medical. JD no longer suffers anxiety about when her next joint is going to sublux, because she knows she can get Prolotherapy to treat future injuries. The peace of mind that comes with Prolotherapy for JHS and EDS patients goes a long way.

CONCLUSION

Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome are both heritable disorders of connective tissue (HDCT) characterized by joint laxity and hypermobility. The conditions are both genetic disorders of collagen synthesis, where the adverse effects of tissue laxity and fragility can give rise to clinical consequences that resonate far beyond the confines of the musculoskeletal system. Both conditions have as their hallmark generalized hypermobility which can affect almost every bodily system. The hypermobility can be documented by the Brighton criteria which involves the objective measurement of the hyperextensibility of various joints. While the major presenting complaint of JHS and EDS is arthralgia in multiple joints, if the hypermobility is left unchecked, joint dislocations and degeneration may prevail. While traditional medical treatments, including education and lifestyle advice, behavior modification, physiotherapy, taping and bracing, exercise prescription,

functional rehabilitation and pain medications offer some symptomatic control, they do little in regard to curbing the progressive debilitating nature of the diseases. The excessive joint mobility, with its subsequent joint degeneration and multiple joint dislocations, can then lead the individual to seek out surgical intervention, which has suboptimal results in the hypermobile patient population versus the normal population. As such, some patients with JHS and EHS are seeking alternative treatments for their pain including Prolotherapy.

Prolotherapy offers great hope for those with symptoms from generalized hypermobility because it is designed to successfully treat the ligament and tissue laxity that accompanies JHS and EDS. Some of the rationale for using Prolotherapy for patients with EDS and JHS are that it has a high safety record, is comprehensive (all or most joints can be treated at each visit), is an outpatient procedure, is cost effective (compared to surgery), pain relief is often quick, and it provides joint stabilization. Perhaps its greatest asset is the fact that this one treatment modality can handle most of the painful musculoskeletal conditions that occur in individuals with EDS and JHS. Prolotherapy could also contribute to the treatment of hypermobility disorders also by preventing the development of precocious osteoarthritis. It has long been known that individuals with JHS and EDS suffer with premature osteoarthritis in various joints and the amount of degeneration correlates with the extent of the individuals hypermobility. The combination of extreme hypermobility and repeated injury is presumed to be what leads to the early osteoarthritis. This is most likely the reason that the hypermobility type of Ehlers-Danlos Syndrome is the most debilitating form with respect to musculoskeletal function.

While the primary author has twenty years experience treating JHS and EDS musculoskeletal symptoms with Prolotherapy, future studies will need to be conducted to best document the exact role Prolotherapy has in the treatment of the musculoskeletal symptoms and hypermobility of JHS and EDS and if it can prevent future joint degeneration in these individuals. ■

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WONDER WHY?

Prolozone™ – Regenerating Joints and Eliminating Pain

Frank Shallenberger, MD, HMD, ABAAM

ABSTRACT

Prolozone is a technique that combines the principles of neural therapy, Prolotherapy, and ozone therapy. It involves injecting combinations of procaine, anti-inflammatory medications, homeopathics, vitamins, minerals, proliferatives, and ozone/oxygen gas into degenerated or injured joints, and into areas of pain. This article reviews the nature of what medical grade ozone is, how it works in biological systems, and how it can be used to regenerate joints and other damaged tissues, and to alleviate pain. Three case studies are presented.

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KEYWORDS: oxygen, ozone, Prolotherapy, Prolozone.

THE BASICS

Prolozone is a technique that marries concepts from neural therapy, Prolotherapy, and ozone therapy. It involves injecting various combinations of procaine, anti-inflammatory medications/homeopathics, vitamins, minerals, proliferatives, and a mixture of ozone/oxygen gas into degenerated or injured joints, and into areas of pain. The result of this combination is nothing short of remarkable in that damaged tissues can be regenerated, and otherwise untreatable pain can be permanently cured. The purpose of this article is to provide insight into what Prolozone is, and how it works. Let's start with ozone.

OZONE = TRIATOMIC OXYGEN

Oxygen is an atom that cannot exist in a stabilized form as a single atom. This is because it does not have enough electrons to balance it out. So in order to provide stability, two oxygen atoms bond together in close proximity and share electrons. This molecule, called O2, is what is generally referred to when the word "oxygen" is used. O2 is the stable form of oxygen that exists in the atmosphere.

When an energetic force, such as electricity (lightening) or ultra-violet light (solar exposure), is imposed upon a molecule of O2, the two oxygen atoms are temporarily split apart into single oxygen atoms. Then, in a matter of nanoseconds these highly unstable oxygen atoms will pair up again and reform back into O2 molecules. But a small percentage of them will unite in a ménage-a-trio known as ozone. Thus, ozone, referred to as O3, is a gaseous molecule which consists of three oxygen atoms all sharing the same electrons.

This is exactly what happens in a corona discharge ozone generator. Oxygen (O2) molecules go into the generator and are exposed to an electric spark. What emerges from the other end is a mixture of oxygen and ozone. The parameters of the generator can be set to produce a given amount of ozone in that mixture. In clinical circumstances the concentration of ozone in the final gas mixture is between 1-3%. In the therapeutic sections of this article I will be using the word "ozone" to refer to this mixture of ozone and oxygen.

Ozone is a relatively unstable molecule. This is because there just are not enough electrons to go around to keep three oxygen atoms stabilized. There are enough for two atoms, but not three. This instability is exactly why ozone is so powerful—because it is driven to give off the extra oxygen atom so that it can be reduced to the stable O2 form. This of course requires getting electrons, and the best place for a single oxygen atom to get an electron in a cellular environment is from the double bonds found in lipids and amino acids. The reaction looks like this:

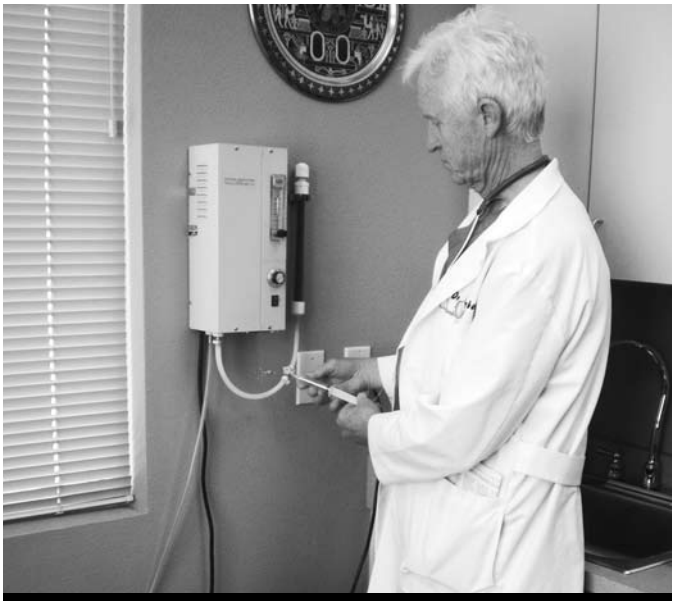
$$O3 + \text{-}C{=}C\text{-} \rightarrow \text{-}C\text{-}O3\text{-}C\text{-} \rightarrow \text{-}CO\text{-}CO2 \rightarrow \text{-}C{=}O + \text{-}C\text{-}O2$$

The resulting peroxides (- C-O2) are short chained, and can easily penetrate cellular membranes. There, they will exert their oxidizing effect on NADH by accepting its electrons, and thereby oxidizing it to NAD. The importance of this reaction will be discussed later. However, this is not the only reaction that can occur with ozone. As I mentioned above, it can also react with itself

to be converted back into oxygen. In a matter of only minutes, ozone molecules can react with each other to form the more stable O2 molecule:

03 + 03 → 302

This process is referred to as dismutation. It does not happen when ozone is injected into tissue, but it does happen when ozone is kept in a syringe. It has been found that in a glass container at room temperature ozone will dismutate at a rate of 50% every 45 minutes. In a plastic container it will dismutate even faster, at the rate of 50% every 30 minutes. This is important to know because once ozone has been generated for a medical application; it must be used rather quickly. It can't be stored and used later. As you can see, this fact somewhat limits the usefulness of ozone. I just can't give my patient a bottle of ozone to take home with him, because within hours it will all have dismutated back into O2.



Dr. Shallenberger filling up a syringe with ozone.

An important precaution to note here is that, with the exception of ozone generators that are strictly used for air or water purification, in no case should ozone destined to be used for medical applications ever be made from room air! The reason is that room air contains 20% nitrogen, and when this nitrogen passes through the energy chamber, it is converted to nitrous oxide and nitric oxide, both of which are toxic in even small doses. So it is imperative that only high quality pure oxygen be used to generate the ozone used for medical purposes.

OXYGEN UTILIZATION

Before I delve into the next section, I need to define the term oxygen utilization. Oxygen utilization quite simply refers to how efficiently a cell or cells are converting oxygen to energy. Decreased oxygen utilization therefore refers to a condition in which oxygen is being less efficiently converted into energy.

When a molecule of oxygen reaches a cell (specifically the mitochondria of the cell) there are two possible ways that it can be metabolized. One, in aerobic metabolism it can interact with either glucose or fatty acids to produce energy. Or two, it will be converted into free radical molecules. In a state of decreased oxygen utilization, more of it will be directed towards free radical production, and less towards energy production. This of course leads to a lethal one-two punch to the cell. It has less energy to maintain itself, and it is being increasingly burdened with free radical injury. Decreased oxygen utilization is at the root of all chronic disease, and I believe is also the fundamental cause of chronic pain and tissue degeneration.

PROLOZONE HISTORY

In 1983 I went to a four day training seminar in Germany on the use of ozone in medicine. One of the things that I learned was that ozone was very effective when injected into rheumatic joints. Inflammation decreased, swelling decreased, and most importantly pain decreased. How and why all this was happening was not explained, but the procedure had been done for years, and several clinical studies had verified the effect.

As so often happens after we learn something, shortly after the seminar I had a patient with rheumatoid arthritis show up at the clinic with severe inflammation and pain in both of her knees. After explaining to her what I had learned, she consented, and I injected both of her knees with ozone gas. The result was dramatic. Within two days 75% of the pain and inflammation was gone. But this case is only the beginning of the story.

The following week a neighbor of this patient came to the clinic asking to have her right knee injected with "the same thing you gave Mary." Only this patient did not have an inflammatory condition. She had an osteoarthritic knee that she had been suffering with for several years. I explained to her that treating an inflamed joint was very much different from treating a degenerated joint, and

although Mary had a good result, I did not know if the treatment would be helpful in her particular case. I told her that as far as I knew, no one had reported any success in treating degenerative conditions with ozone.

Then she asked, "Well will it make me any worse? I can hardly walk as it is. They already want me to have a total knee replacement. What harm could it do to try?" I had to admit that she had a good point, so I consented to the proposal.

She called me up one week later and told me that she was 20% better, and would I please give her another injection. We continued the treatments for a total of seven times, at which point she was so functional that she saw no need for further treatments. She remained that way for months, and only needed to return 2-3 times each year for a "booster." Soon, she told several other people about her success, and I began using the treatment on a host of other patients.

One of those patients, after her third injection, asked me a question. "Doctor, these injections really hurt a lot. Why don't you use any Novacaine?" It's true. When ozone is injected into tissue, especially in the higher concentrations that I was using at the time, it causes intense pain for the first few minutes while it is exerting its oxidizing effects. After 3-4 minutes, the pain is almost completely gone, but those first few minutes can be rough.

In addition to its pain blocking effects, as any student of neural therapy knows, procaine (the generic form of Novacaine) also stabilizes and restores damaged membrane potentials. This effect often results in curing chronic pain with nothing more than simply injecting procaine into the damaged area. For both of these reasons, the next time I injected this patient I pre-injected the knee with buffered procaine. The result was just as good as what I had been seeing when using only ozone, perhaps even better, and now I had a much happier patient. I continued to use this combination.

Then I thought since I was already pre-injecting the area with procaine, what else might I put into the mix that might make the results even better? I reasoned that ozone was exerting its healing effect through the process of improving oxygen utilization, so I added various nutrients that play important roles in the utilization of oxygen. This included magnesium, niacin, methycobalamin, folic acid, and pyridoxine. I also experimented with using sea salts. Soon, I discovered a combination of ingredients that was easy to administer, inexpensive, and definitely improved my results. But I was not finished.

I also knew that many of the patients I was treating were suffering not only from pain stemming from degeneration, but also pain from inflammation. The two were often combined. This became very obvious to me after treating several cases in which the patients had been previously treated with injectable corticosteroids. The previous use of steroids not only did not interfere with ozone therapy, in some cases it actually seemed to help the process along. So I made a homeopathic dilution of methylprednisolone, and began adding it to the pre-injection mixture. To this I also added an anti-inflammatory homeopathic combination called Traumeel™. My results continued to improve. But something else also occurred to me.

All along, I had been wondering if these injections of ozone weren't simply another version of Prolotherapy. After all, ozone is an irritating substance, and it hurt. Perhaps it was working in the same way that a proliferative solution worked. But proliferative solutions require inflammation in order to be effective, and I was now discovering that ozone injections worked even in the face of anti-inflammation therapy. So just to further check this out, I started using allopathic doses of methylprednisolone in the pre-injection. I also experimented with using oral prednisone in combination with the ozone treatments. What I discovered was that the effects of ozone therapy, unlike those from proliferative agents, was not interfered with by anti-inflammatory medications. Indeed, they seemed to be synergistic.

This simple observation caused me to theorize that ozone therapy was working along a principle that was different from the way that Prolotherapy works. I will explain what I think this principle is in the next section. But if that is the case, if they are both working from two different principles, might it not be reasonable to expect that there may be some synergistic effect from combining ozone with Prolotherapy? So that's what I did. I developed a protocol wherein when I initially began treating a patient I used an anti-inflammatory mixture for the first 2-3 times. Then, when inflammation was no longer part of the clinical picture, I started adding in various proliferative agents. The one that I have the best results with is sodium morrhuate.

HOW DOES PROLOZONE WORK?

If Prolozone is not working simply as another form of Prolotherapy, how is it working? The answer to this question came to me one day as I was talking with a friend and colleague David Edwards, MD. Dave is a cardiologist, and the conversation was about myocardial hibernation. Myocardial hibernation is a term used to describe the condition in which there is a localized decrease in cardiac function due to localized ischemia. Restoration of normal coronary flow (e.g., by coronary bypass, chelation therapy, etc.) will restore normal function in the affected region. In other words, it is a localized area of tissue that is trapped in a state of reduced oxygen utilization. Restore oxygen utilization, and the tissue will function normally again.

This same principle also applies to cases of cerebral infarct. Between the area of dead brain tissue and healthy tissue, there is a localized penumbra of brain tissue that is trapped in a state of decreased oxygen utilization. This tissue is not dead, but it is non functional. Restoring oxygen utilization to these cells with hyperbaric oxygen will often result in significant clinical improvement. I believe that Prolozone works by improving oxygen utilization in a localized area of damaged connective tissue, allowing it to heal, and to restore full function.

WHAT CAUSES CHRONIC PAIN?

We damage our connective tissues all the time. This is normal. In fact, it is controlled damage that is at the very heart of why exercise is so beneficial. When the tissue is damaged, stem cells and blast cells are called to the area of injury. Growth factors are stimulated, and very soon the damage is repaired. You sprain your ankle, and then it heals. You break your neck, and then it heals. That is, unless it doesn't.

Why is it that some injuries never heal, and go on to become areas of chronic pain and dysfunction? What happened to the healing mechanisms that always worked before? I think it's the same process as myocardial hibernation and cerebral penumbra of injury. I believe that these localized areas fail to heal because of a localized decrease in oxygen utilization. Reverse this, and an area of chronic pain will become normal again. Reverse this, and an area of chronic degeneration will begin to regenerate exactly as it was supposed to in the first place.

Here's another question. Why does chronic pain and degeneration only occur in joints and ligaments instead of other tissues? And why do people heal so much more reliably when they are young than when they become older? The answer in both cases has to do with decreased oxygen utilization.

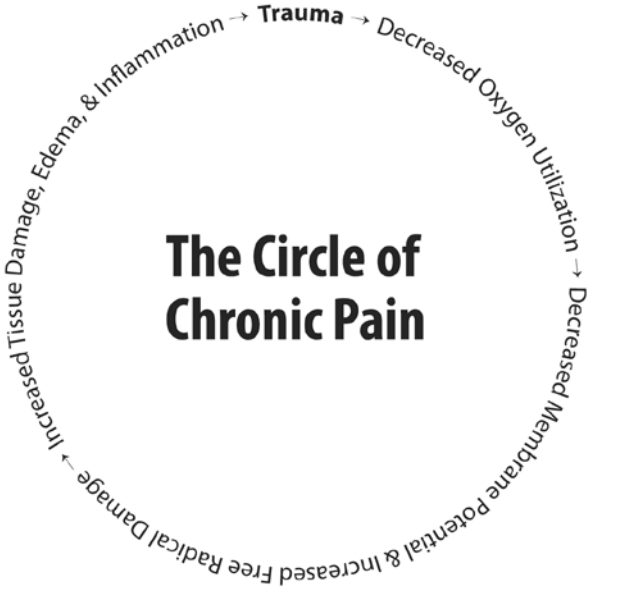
Ligaments and joints are notoriously known as areas of decreased oxygen tension. The oxygen tension in a healthy ligament is often only $1/10^{th}$ that of the tissue only several millimeters away from it. The same is true for joints. These areas are setups for developing a situation that involves a localized area of decreased oxygen utilization.

But as we grow older, does our circulation improve, or does it decrease? Of course it decreases. So the natural decrease in oxygen utilization that is seen in the healthy ligaments and joints of the young become even further compromised with aging. So here's the scenario for chronic pain and tissue degeneration that seems to correlate well with what I have clinically seen from using Prolozone in thousands of patients over these past 20 years.

There is a naturally occurring decrease in circulation to ligaments and joints. This condition is further compromised with aging. The result is a naturally occurring localized decrease in oxygen utilization in these tissues. Then along comes a trauma. The trauma produces edema and inflammation causing a further localized decrease in oxygen utilization. This decrease in oxygen utilization produces a localized increase in lactic acid production, free radical damage, and necrosis which serves as the foundation for sensory irritation and injury, all of which causes chronic pain.

Both the initial trauma and the ensuing edema and inflammation result in a decrease in circulation. This compromises the delivery of oxygen and important nutrients to the localized area of damage, and decreases oxygen utilization even more. The trauma also compromises cell membrane potential, which both causes decreased oxygen utilization, and in turn is caused by decreased oxygen utilization. So, even though stem cells and blast cells are there, and growth factors are being released, healing does not occur. None of these mechanisms can be effective because of a lack of adequate oxygen utilization. Thus, a vicious cycle, which I dub "The Circle of Chronic Pain" results: decreased oxygen utilization leads to a decrease in cell membrane potential and an increase in free radical

damage, which leads to tissue damage and increased inflammation and edema, which perpetuates the trauma, which leads to a further decrease in oxygen utilization. All of which adds up to chronic pain and degeneration. Break that cycle, and the cells and tissues can begin to do what they usually do so well—heal themselves. That is precisely what Prolozone does.



The circle of chronic pain. Prolozone heals this cycle of chronic pain, allowing the cells and tissue to regenerate and heal.

Each component of Prolozone has a specific biological purpose. Procaine acts to re-establish cellular membrane potentials. Anti-inflammatory agents decrease edema and swelling. The inclusion of vitamins and minerals provides necessary substrates for oxygen utilization that in damaged tissues are often deficient. And finally, oxygen utilization is directly stimulated by ozone.

How does ozone stimulate oxygen utilization? The answer to this question is beyond the scope of this article, but is answered in my book, *The Principles and Applications of Ozone Therapy – A Practical Guideline For Physicians*, which can be purchased from Amazon.com. The short answer is that is does it by oxidizing NADH to NAD.

As oxygen utilization decreases, in this case from trauma, the ratio of NAD to NADH decreases. A decrease in the cells' NAD/NADH ratio results in a slowdown of all cellular function including protein synthesis, cellular division, growth factor function, membrane potential maintenance, etc. As previously mentioned, ozone reacts with the double bonds in lipids and amino acids and creates peroxides that are able to oxidize NADH to NAD, and thereby correct the declining NAD/NADH ratio. And by doing this, cellular function is stimulated to return to business as usual, and oxygen utilization is returned to normal. The net result is that the tissues get what they need to heal—energy. And as they heal, the circulation to the area is re-established, pain is cured, and the treatment is complete.

OTHER LOCALIZED EFFECTS OF OZONE

As a powerful oxidizing agent, ozone also has several other effects that are important for tissue repair and regeneration. One is by stimulating growth factor production and release. One paper published in 1996 examined the critical role that protein tyrosine phosphorylation events play in proliferation and differentiation. The authors determined that oxidizing agents "stimulate growth response events in vascular smooth muscle cells," and also "stimulate tyrosine phosphorylation of several proteins including epidermal growth factor receptor." The stimulation of growth factors, especially endothelial factors are important for tissue regeneration to occur.

But ozone therapy can do more than just stimulate growth factor production and release. It also activates the membrane receptors through which growth factors exert their effects. For example, a paper published in the *Journal of Biological Chemistry* established a novel role for the mitochondrion as a proximal target specific to oxidant induced signaling and growth factor transactivation.

And finally, there is evidence that ozone therapy can mediate the effects of the various growth factors. A recent 2005 paper entitled, "NAD(P)H Oxidase 4 Mediates Transforming Growth Factor-ß1–Induced Differentiation of Cardiac Fibroblasts Into Myofibroblasts," describes how oxidized nicotinamide adenine dinucleotide (NAD) induces circulating fibroblasts into repairing damaged cardiac tissue. NAD activity is enhanced by ozone therapy because it increases the NAD/NADH ratio.

IT'S A GAS!

One last note about the effect of injecting a gas. Unlike injecting a liquid, which will just pool in the area of injection, gases expand when injected, and dissect along areas of inflammation. This fact is exploited in the Prolozone technique by injecting large volumes (10-30cc)

of gas into each treated area. The effect is that very large areas, and difficult to reach areas are treated with only one injection. This decreases the number of injections needed to treat a given area, and also greatly decreases the chance of missing the area of primary involvement. I call it, "Target practicing with a shot gun."

WHAT A PROLOZONE PATIENT CAN EXPECT

The first thing that most patients notice after a Prolozone treatment is an almost immediate 50-80% decrease in pain. This is in part due to the effect of the procaine. But ozone itself has a significant ability to directly relieve pain. A 2009 article published in the *European Journal of Pharmacology* demonstrated that a single subcutaneous injection of ozone prevents allodynia and decreases the over-expression of pro-inflammatory caspases in the orbito-frontal cortex of neuropathic mice, immediately eliminating any signs of pain. Lamberto Re, a medical doctor and soccer team physician in Verona, Italy routinely injects the acutely injured areas of his players with ozone alone. He does not use procaine. And he reports a marked decrease in pain as well as an improved rate of healing.

Next, chronic areas of degeneration such as in osteoarthritic knees, hips, and ankles will regenerate. Although more research is needed to fully document this effect, some physicians have already taken pre and post treatment x-rays that have shown an increase in cartilage thickness in knees treated with Prolozone. And fortunately, other than a rarely occurring and temporary increase in pain in the area injected, no significant side effects from Prolozone have ever been demonstrated. Other than the possibility of an allergy to one of the liquid components, there are no contraindications to its use.

CONDITIONS THAT RESPOND

The primary criterion for selecting a patient for Prolozone is pain. If it hurts, Prolozone should be tried. I have had cases in which the chief complaint was instability, and the patient had no complaints of pain. A classic example would be a recurring dislocating shoulder. Whereas Prolozone has worked well in many of these cases, my experience is that it should be combined with classical Prolotherapy for best results.

The following is a list of conditions that have been found to be very responsive to Prolozone: chronic neck and back pain from any cause, rotator cuff injuries, degenerative and arthritic hips, knees, and ankles, degenerated discs, plantar fasciitis, carpal tunnel syndrome, TMJ, sciatica, heel spurs, neuromas, tennis elbow, sinus infections, pelvic disorders, dental infections, post-op pain, non-union fractures, painful scars, and sports injuries—basically anything that hurts. (*See Table 1.*)

Conditions responsive to Prolozone

- Carpal tunnel syndrome
- Chronic back pain
- Chronic neck pain
- Degenerated discs
- Degenerative & arthritic ankles
- Degenerative & arthritic hips
- Degenerative & arthritic knees
- Dental infections
- Heel spurs
- Neuromas
- Non-union fractures
- Painful scars
- Pelvic disorders
- Plantar fasciitis
- Post-op pain
- Rotator cuff injuries
- Sciatica
- Sinus infections
- Sports injuries
- Tennis elbow
- TMJ

Table 1. Conditions that have been found to be very responsive to Prolozone.

While clinical trials using the exact technique involved in Prolozone have not been published, there have been several papers published in the international literature lauding the use of ozone injections in various pain syndromes. A list of these articles is provided at the end of this article.

ADVANTAGES OF PROLOZONE

I am a big fan of classical Prolotherapy and neural therapy. These are the techniques that I originally learned years ago, and they are very effective. They set the stage for the development of the various Prolozone techniques. However, at this point, simply because Prolozone is so effective, I virtually never use these other modalities as they are classically used. Additionally, Prolozone offers some advantages over classical proliferative therapy.

First and foremost, ozone directly stimulates the down regulated oxygen utilization in damaged areas of the body that is at the heart of why these areas don't heal. Prolotherapy does not have this action. Secondly, Prolotherapy is typically very painful, with the pain from the therapy often persisting for days to weeks after a treatment. In contrast, patients receiving Prolozone feel immediate improvement, with very little or no pain at all during or after the treatments.

Prolotherapy requires many injections, whereas Prolozone only requires a few. This means that Prolozone is faster, and typically much less expensive.

Because Prolozone involves the injection of a gas in large volumes which expands into a large area of surrounding tissue, it is not as critical to pinpoint each Prolozone injection as it is when using proliferatives. Thus, it is easier to master.

Since Prolozone does not work as a proliferative, the use of anti-inflammatory medications is not contraindicated, and can in fact be synergistic.

Prolozone is especially effective when used intra-articularly. It can stimulate the regeneration of damaged cartilage in knees, shoulders, ankles, and hips.

CASE EXAMPLE #1

Mary Anne is a 48 year old master ICU nurse. 10 years prior to her visit she injured her back in a lifting accident. After a year of failed conservative management, she had a lumbar spinal fusion involving the placement of several metal plates. Her pain continued, and was managed with narcotics. Several years later for no apparent reason her neck began to hurt, and she developed right arm neuropathy. Her neck was then fused, and metal plates placed there as well. Shortly after, she was forced to stop nursing.

Previous to my seeing her, she had had neural therapy, classical Prolotherapy, acupuncture, and various physical therapy techniques. All of these modalities had failed to offer anything but temporary relief. On her first visit she presented as a woman addicted to narcotics, with chronic and severe pain in her neck, down her right arm, in her lower back, and down both legs. She also was developing increasing weakness in her right hand. She was only able to ambulate into the treatment room with assistance.

She was treated with Prolozone injections to her neck and lower back every two weeks for three months. The treatments took about 10 minutes. At this point the weakness in the hand had disappeared, and her pains had diminished to the point that she had cut her medication dose in half. Her treatments were decreased to three week intervals, and after three more months her pain had reduced to a fraction of what it had been, and she was off all medication.

COMMENT

This was obviously an extreme case, but she is a great example of what Prolozone can do. Most cases of chronic back or neck pain resolve in 4-6 treatments. This patient went on to have several relapses of her pain, primarily because she had to make frequent flights across the country. It was not until a full year of therapy, with treatments being performed at six week intervals that she became completely functional with minimal pain. It has now been almost one year since her last treatment and she continues to do well.

CASE #2

Joe is a 66 year old retired metal worker who presented with bilateral knee pain. His x-rays showed bilateral medial compartment bone on bone. He had been advised by orthopedic surgeons to have bilateral replacements. He was very limited in his activities, could no longer play golf, and walked with a slow, shuffling gait. He took NSAIDs daily.

Joe was treated with intra-articular Prolozone every two weeks for three sessions. At that point he was no longer requiring medication, and was able to perform activities that he previously could not do. The treatments were stretched out to every 3 weeks and then every 4 weeks, and ultimately every 6 weeks until he was completely asymptomatic and playing golf again. He had a total of eight treatments.

COMMENT

I have seen many cases just like Joe's. About 85% of the time they have the same kind of result. I have never had a patient go to knee surgery in fifteen years of using Prolozone. *Figure 1* is an x-ray of another patient (not Joe) taken in August. *Figure 2* was taken the following February after eight Prolozone treatments. I wish I had more x-rays like this, but I don't routinely take post therapy x-rays. These were done by a colleague trained in the Prolozone technique.

CASE #3

Randy is a 67 year old retired plumber. I was treating his wife for a rotator cuff injury, when on her third visit he told me the following. "Doc, my wife is doing so well that I thought maybe you can help me too. Nobody else

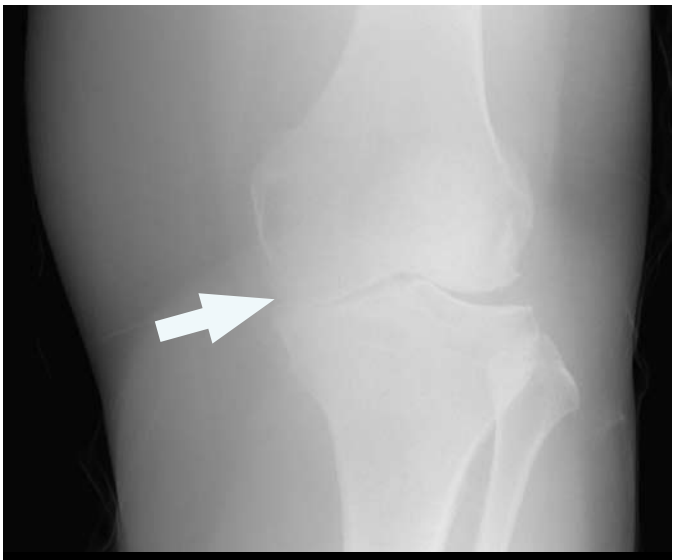


Figure 1. Knee X-ray before Prolozone™ showing severe medial joint space narrowing.

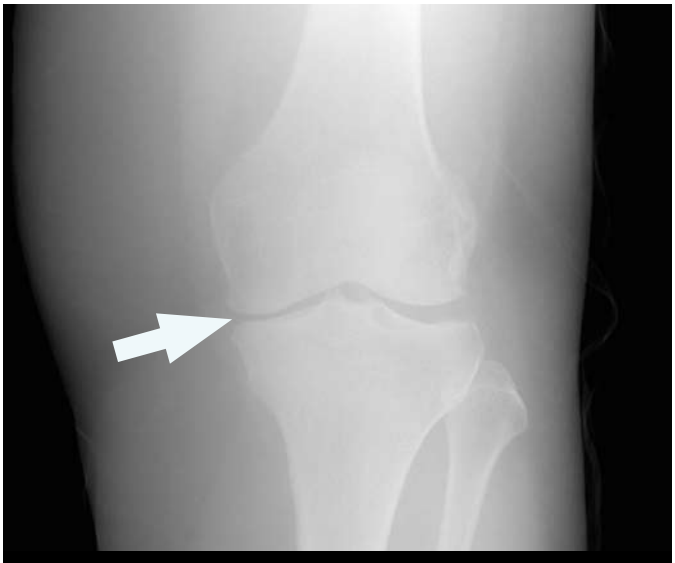


Figure 2. Knee X-ray after Prolozone™ showing increased joint space.

can. About 12 years ago I was wrenching a pipe when the wrench slipped and the back of my right hand was slammed hard against a piece of metal. Nothing was broken, but I have had severe pain which limits the use of my wrist ever since then. I more or less just ignore it, but I am unable to do certain things like reach over and pick up a bag because of the pain."

Randy's examination revealed pain on stressing the wrist, and tenderness over the affected area on the dorsum of the wrist. It took me all of five minutes to infiltrate the area with Prolozone. When Randy returned with his wife four weeks later, he happily reported that the pain was completely gone. It has now been 1½ years since that first injection, and he remains asymptomatic.

COMMENT

What? A chronic pain that goes away with only one inexpensive five minute treatment? Sounds like an exaggeration. But I have seen this kind of thing happening so often that I am convinced that ozone has properties for alleviating chronic pain which are unique, and still not fully understood. But don't believe me. Call up any one of the doctors using Prolozone. They will tell you they see the same kind of remarkable results.

JOIN THE AMERICAN ACADEMY OF OZONOTHERAPY

I have been training doctors in the Prolozone technique for over fifteen years. Of course the ones who learn the fastest are the ones who are already versed in classical Prolotherapy, and/or are used to injecting tissue. Because of their understanding of anatomy, orthopedists, osteopaths, and chiropractors are particularly quick learners. But anyone can do this therapy. It is a very forgiving modality. Remember, it's like target practice with a shotgun. It's hard to miss the bull's eye.

This January, 2011, The American Academy of Ozonotherapy (AAO) was formed. The AAO is an academy of health professionals dedicated to establishing standards for the art and science of Ozonotherapy, educating the public and other health professionals about the many uses of Ozonotherapy in medicine, and promoting research in Ozonotherapy. Our goal is to enhance the health and well being of people through this safe, inexpensive, and effective therapy. You can learn more about the AAO at www.aaot.us.

For information on Prolozone training and joining the AAO, please contact me at doctor@antiagingmedicine.com. ■

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8. Bonetti M, et al. Intraforaminal O(2)-O(3) versus periradicular steroidal infiltrations in lower back pain: randomized controlled study. AJNR Am J Neuroradiol. 2005 May;26(5):996-1000.

   CONCLUSION: Ozone more effective than steroids – 8.6 vs 21.4% poor outcomes.
9. Fifth International Symposium on the Applications of Ozone, April 2007, Havana, Cuba.

   CONCLUSION: We conclude that intra-articular ozone is an effective therapy in the treatment of grade III knee osteoarthritis resistant to treatment with NSAIDs.

   "Ozone Shot as Effective as Surgery for Herniated Discs" As reported in CyberRounds, by Neil Wagner online at www.cyberrounds.com.

   A Toronto team examined the results of 12 previous studies involving over 8,000 patients of ozone treatment of herniated discs. The studies showed ozone therapy to be just as effective as surgery but with a shorter recovery time and a much lower risk of complications.

WONDER WHY?

Neural Prolotherapy

Adam D. Weglein, DO, DABMA

ABSTRACT

There are many new developments in the world of regenerative Orthopedic Medicine. One innovative treatment option is called Neural Prolotherapy. Traditional Prolotherapy has focused on ligament-tendon healing, and has shown to be a powerful treatment modality. With Neural Prolotherapy, however we shift our focus to the subcutaneous nerves as a source of pathology. These subcutaneous nerves in a pathologic state can lead to neurogenic inflammation and pain. We introduce and explore the use of low dose dextrose Prolotherapy in the treatment of neurogenic inflammatory pain. Neural Prolotherapy is indeed a fantastic treatment option that has the potential to further our healing profession.

Journal of Prolotherapy. 2011;3(2):639-643.
KEYWORDS: Neural Prolotherapy, Neurofascial Prolotherapy, neurogenic inflammation.

PERSONAL BACKGROUND

Prolotherapy or Proliferation Therapy stimulates regeneration and repair of injured tissue with the use of dextrose and other agents. I was introduced to Prolotherapy during my Sports Medicine fellowship at South Pointe- Cleveland Clinic by Dr. Zenos Vangelos (Program Director Sports Medicine Fellowship, SP-Cleveland Clinic). I was first introduced to the concept of Neural Prolotherapy by Dr. Dean Reeves. I subsequently traveled to Ferrara, Italy to obtain training from Dr. John Lyftogt in Neural Prolotherapy.

BRIEF HISTORY OF NEURAL PROLOTHERAPY

Neural Prolotherapy also called Neurofascial Prolotherapy (NPT) is one of the newest advances in Regenerative Orthopedic Medicine. Neural Prolotherapy is not to be confused with traditional "German" Neural injection therapy. German Neural therapy is a great treatment option using procaine to treat interference fields and scars.[13] I regularly treat my patients with scars using this German Neural therapy technique.

Neural Prolotherapy (NPT) was primarily born out of clinical observations and involves the treatment of neurogenic inflammation. Neural Prolotherapy has its roots dating back to 1989 with Dr. Paul Pybus and Dr. Roger Wyburn-Mason, in their book "Intraneural Injections for Rheumatoid Arthritis and Osteoarthritis." In the book Dr. Pybus explains the concept of neurogenic inflammation as it relates to osteoarthritis.[14]

PATHOLOGY OF NEUROGENIC INFLAMMATION

The pathology of neurogenic inflammation is well established.[1, 2, 16] Ligaments, tendons and joints have TRPV1-sensitive C pain fiber innervation. Dr. Pybus explains that the C pain fibers transmit the "deep pain" often seen with osteoarthritis.[14] "When these C pain fibers are irritated anywhere along their length they will transmit ectopic impulses in both forward (prodromic) and reverse (antidromic) direction."[14] The forward direction of the nerve signal will cause pain perception as the signal travels through the posterior root ganglia up to the brain. You will also have a local reflex action from the spinal cord ventral horn cells out to the muscle fibers, which will cause a reflex muscle spasm.[14] The reverse (antidromic) signal will travel to the blood vessels where substance P is released causing swelling and pain. The nerves themselves also have a nerve supply called the Nervi Nervorum (NN).[2] In a pathological state, the NN can release substance P (Sub P) and Calcitonin Gene Related Peptide (CGRP) onto these C pain fibers.[11] Sub P and CGRP are known to cause pain, swelling of the nerve and surrounding tissue.[7]

Dr. Pybus treated this above neurogenic inflammation with lidocaine and steroid injections. Dr. John Lyftogt and Dr. Dean Reeves expanded on Dr. Pybus' work adding the dextrose Prolotherapy concept. Dr. Lyftogt noticed that these same nerves responded even better to a low dose dextrose injection. He will be expanding on this further in his upcoming book. Dr. Lyftogt discussed in his recent Neural Prolotherapy meeting that "Cutaneous nerves pass through many fascial layers on their way to the spine. When there is neurogenic swelling at the Fascial Penetration Zone, a Chronic Constriction Injury (CCI) occurs. The CCI points will inhibit flow of Nerve Growth Factor (NGF).[8, 7] Proper flow of NGF is essential for nerve health and repair."[3] (*See Figure 1.*)

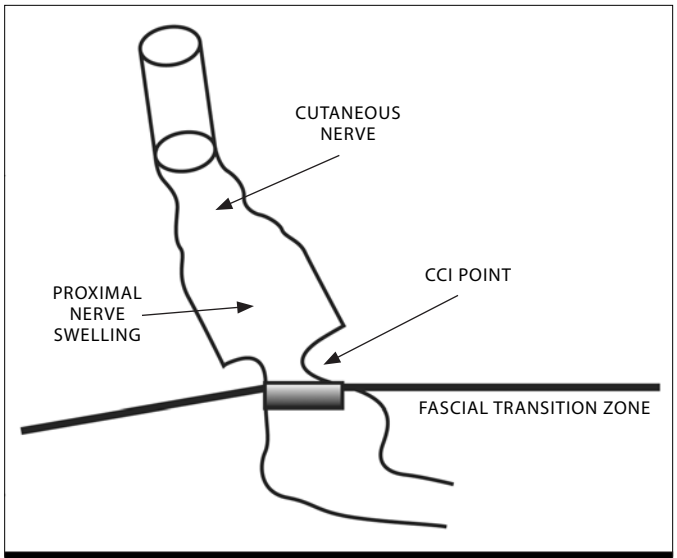

Figure 1. Cutaneous nerve chronic constriction injury.

There are two major ways that the fascial penetration point can affect a nerve. Trauma to a nerve will cause edema to travel proximal and distal to the injury. When this swelling reaches the fascial penetration points this can cause a self-strangulation of the nerve and decrease nerve growth factor flow.[16, 17] Morton's neuroma is a clinical example of this.[17] Dr. Pybus has also suggested that a change in fascial tension from repetitive muscle dysfunction can also cause a CCI point.[15, 17] Another critical concept in NPT is what is called Bystander disease.[9, 17] Bystander disease helps explain how superficial nerve pathology can affect deeper anatomic structures.[9] This is based on Hilton's law. Hilton's law states: the nerve supplying a joint also supplies both the muscles that move the joint and the skin covering the articular insertion of those muscles.[9] An example: The musculocutaneous nerve supplies the elbow with pain and proprioception as it is the nerve supply to the biceps brachii and brachialis muscles, as well as the skin close to the insertion of these muscles.[17] Hilton's Law arises as a result of the embryological development of humans. This concept of Hilton's law coupled with the idea of anterograde and retrograde axonal flow of neurodegenerative peptides,[17] can help explain the wide reaching affects of NPT on pain control.

TREATING NEUROGENIC INFLAMMATION

Clinical observation has shown that a 5% dextrose solution with sterile water will give immediate analgesia. In my experience, this pain control will last from 4 hours to 3 weeks. The proposed mechanism is again a dextrose mediated inhibition of the neurogenic inflammation. Glucose responsive nerves have been demonstrated throughout the nervous system.[4, 5, 6] One proposed mechanism of action suggests that dextrose binds to pre synaptic calcium channels and inhibits the release of substance P and CGRP, thereby decreasing neurogenic inflammation. This allows normal flow of nerve growth factor and subsequent nerve repair and decreased pain.[7]

Dr. Lyftogt has studied the use of a wide range of dextrose, lidocaine, and procaine concentrations. At this point in time, he is using 5% dextrose in sterile water solution (1cc of dextrose 50 in 9cc sterile water). No lidocaine is used. NPT is given just under the skin close to subcutaneous nerves at weekly intervals.

RESEARCH

Dr. Lyftogt's early research focused on the treatment of Achilles tendons. He has treated over 300 Achilles tendons with a success rate of more than 90%. Dr. Lyftogt has published six level 4 studies in the *Australian Journal of Musculoskeletal Medicine* since 2005. He has studied the shoulder, ankle, back, elbow, and hip. His 2 year follow up shows a 80-100% success rate.[10, 11, 12]

PERSONAL EXPERIENCE WITH NEURAL PROLOTHERAPY

I have been using Neural Prolotherapy in my practice for the past year with outstanding results. I find myself often using NPT as my first treatment option, followed by traditional Prolotherapy and Platelet Rich Plasma as needed. My approach is to treat from the superficial to deep tissues. Along with my complete history and physical exam, I now check for swollen and painful peripheral nerves. If the subcutaneous nerves are swollen or painful on examination, this is an indication to treat with NPT.

CASE EXAMPLES

Aforementioned, I now use NPT as a first line treatment on most patients. In the photos, the circles represent the chronic constriction points (CCI) of the superficial nerves. If the CCI points are tender to palpation, they need to be treated to have a successful outcome.

CASE 1: SHOULDER ROTATOR CUFF TEAR AND SUPRACLAVICULAR NEUROGENIC INFLAMMATION

Mr. VF is a 59-year-old male with a complaint of right shoulder pain for the past 7 months. The patient had an MRI of his right shoulder that showed an articular

supraspinatus partial tear 11mm. I used Platelet Rich Plasma (PRP) along with Prolotherapy, 15% dextrose and lidocaine solution, to treat the supraspinatus tendon under ultrasound guidance on 7/26/2010. The patient underwent my post PRP-Prolotherapy physical therapy protocol for 6 weeks. This is a week-by-week incremental increase in physical therapy to enhance the healing benefit of PRP.

On Mr. VF's follow up visit with me on 9/13/10 he reported 85% improvement in shoulder pain and function. His physical exam was full passive range of motion and active range of motion. He did have pain in his shoulder with golf swinging and on palpation over the subcutaneous shoulder supraclavicular nerve. Due to the fact that the patient had pain over the path of the supraclaviular nerve, I decided to treat this nerve with Neural Prolotherapy, 5% dextrose in sterile water. (*See Figure 2.*) He had 4 injections done at that visit along the supraclavicular nerve. The patient had immediate complete pain control, which lasted for 3 days. He followed up at weekly intervals. Each week he had decreased pain and required fewer injections. A total of 3 weeks (3 treatments) of Neural Prolotherapy were done. The patient had complete pain relief in his shoulder and was able to continue golfing pain free.

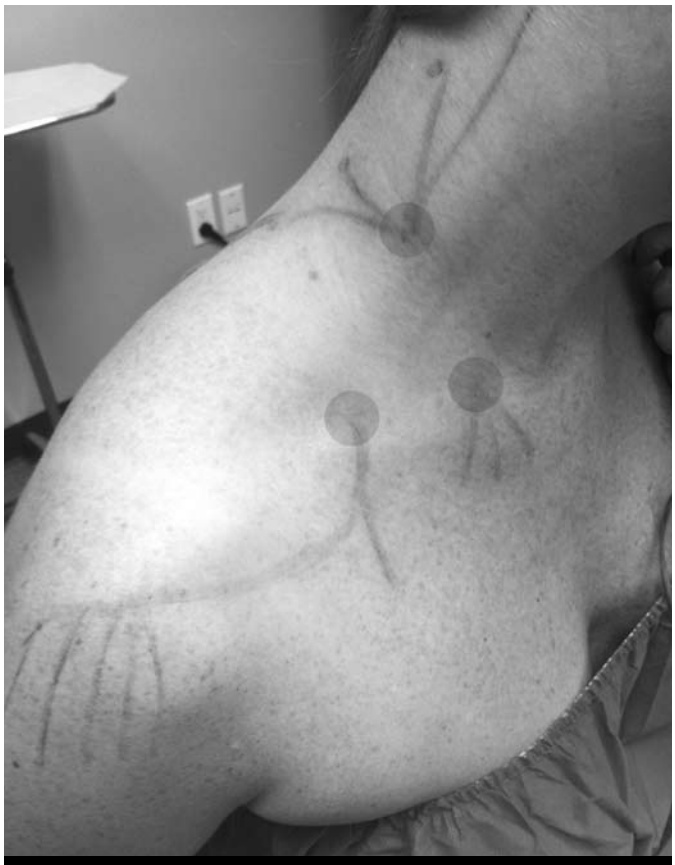

Figure 2. Shoulder supraclavicular nerve neurogenic pain pattern. Neural Prolotherapy eliminates the neurogenic inflammatory component of pain.

CASE 2: LOWER BACK PAIN WITH SUPERIOR CLUNEAL NEUROGENIC INFLAMMATION

Mr. GH is a 50-year-old with a history of lumbar pain for the past 26 years. His pain was located in his lumbar L5 paraspinal area on the left, superficial to the facet area. He had some occasional radicular symptoms down his left leg, however not at the time of presentation to my clinic. He had tried chiropractic treatments, physical therapy. He had an MRI that showed L4/L5 hypertrophy of facet joints. L5/S1 broad 5mm posterior disc protrusion and no thecal sac effacement. In addition, his MRI stated left sided facet hypertrophy moderate and left sided foraminal narrowing. On physical exam the patient had pain on superficial exam of the L4, L5 paraspinal muscles (ventral rami nerves), along with pain on superficial exam of the L1, L2 superior cuneal nerves. (*See Figure 3.*) I decided to use Neural Prolotherapy as a treatment based on pain over these superficial nerves. The patient underwent 5 weekly treatments of Neural Prolotherapy. The lumbar L4 and L5 left sided near ventral rami injections were done with a vertical ½-inch, 27G needle. The left sided superior cluneal L1, L2 were also injected. All injections were done with 5% dextrose in sterile water, 0.5cc injected subcutaneous per site. At his 12-week follow up he was completely free of pain.

CASE 3: KNEE PAIN WITH SAPHENOUS NEUROGENIC INFLAMMATION

Mr. MW is a 57-year-old who had left knee pain for 3 months. His MRI of the left knee showed tricompartment osteoarthritis, medial diffuse degenerative fraying of meniscus, lateral degenerative fraying of meniscus. The patient had most of his pain initially within the knee joint, as morning stiffness. We started treatment for osteoarthritis with intraarticular hyaluronic acid injections (Euflexxa). This gave him only a minor benefit. We proceeded to do a course of Prolotherapy. He had 3 treatments of Prolotherapy. At each treatment, he received Prolotherapy intraarticular, to his medical collateral ligament, and coronary ligaments along his medical meniscus. This provided benefit. To further healing, at his next visit, we proceeded to do Platelet Rich Plasma and Prolotherapy to the coronary medial ligaments, MCL and intraarticular.

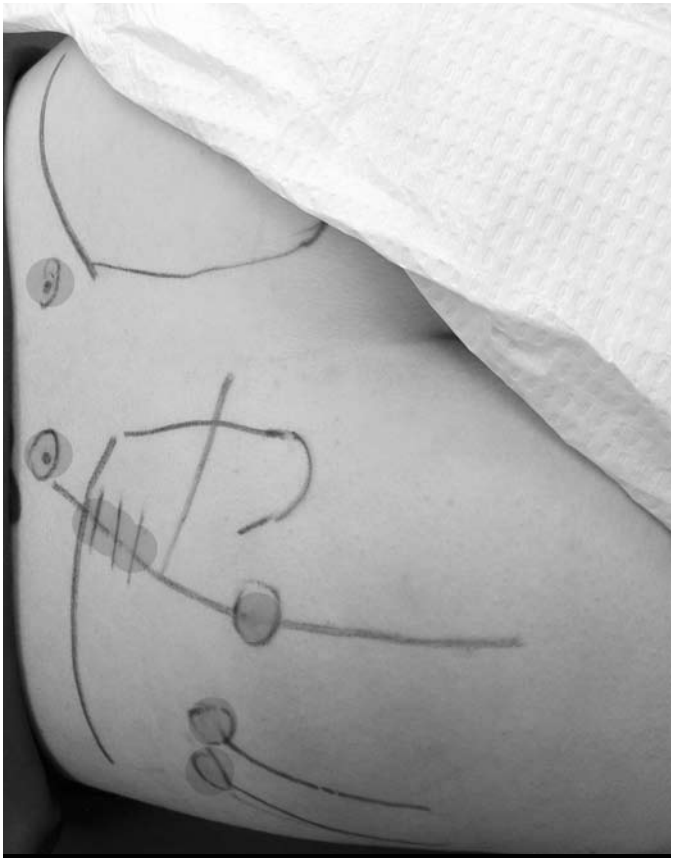

Figure 3. Lumbar spine superior cluneal nerve neurogenic pain pattern.

With his two month post-PRP follow up he had much improved pain control and no locking or giving out of the knee. He no longer had the deep pain within his knee. He did have superficial pain over the knee saphenous nerve; thus, Neural Prolotherapy was done. He had a total of 4 weekly Neural Prolotherapy treatments to the saphenous nerve. On his follow up he was pain free, had full range of motion, and no further treatment was needed.

CASE 4: KNEE PAIN MENISCUS PAIN WITH SAPHENOUS NERVE NEUROGENIC INFLAMMATION

Mr. B O'M is a 46-year-old male with left knee pain for the past 6 months, after injuring his knee playing golf. His MRI showed medial meniscus tear. The patient had undergone two arthroscopic surgeries to try and repair the meniscus tear. On physical exam the patient had pain along his medial saphenous nerve on the left knee. Due to the fact that the patient had pain along the saphenous nerve on physical exam, we started treatment with Neural Prolotherapy to this area. (*See Figure 4.*) He had a total of 4 weekly treatments of Neural Prolotherapy. The patient

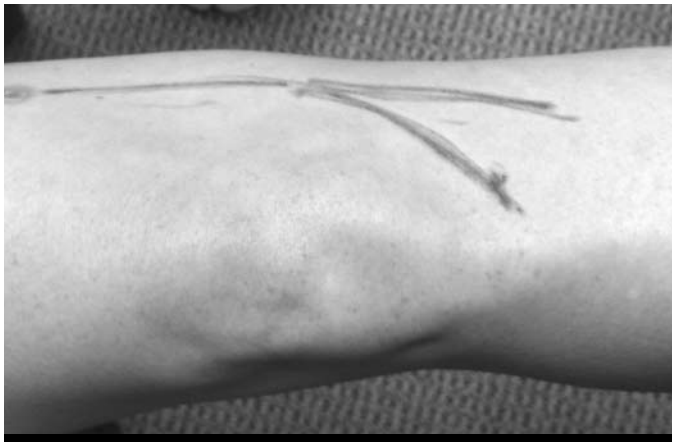

Figure 4. Saphaneous nerve infrapatella branch pain pattern.

reported that the superficial pain over the medial joint line at the location of the saphenous nerve was no longer present, but that there was still a deeper medial knee pain. We proceeded to do traditional Prolotherapy and Platelet Rich Plasma intraarticular and along medial coronary ligaments, which gave him complete pain relief.

I hope these cases help demonstrate the potential use of NPT in Orthopedic Medicine.

As in all forms of medicine, the closer we are to establishing the etiology of disease, the better our treatment outcomes are. When we consider the complexity of musculoskeletal derived pain, we need to address the etiology of pain at its root cause. There are many pain generators such as bone, ligament, tendon, fascial, muscle and nerve. Traditional Prolotherapy and Platelet Rich Plasma have demonstrated their structural healing ability. Now with the use of Neural Prolotherapy we can address the pathology of neurogenic inflammation bringing yet another level to our healing profession. ■

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WONDER WHY?

Sacroiliac 201: Dysfunction and Management

A Biomechanical Solution

Richard L. DonTigny, PT

ABSTRACT

A commonly overlooked, reversible biomechanical vulnerability of the sacroiliac joints (SIJ) makes them subject to injury even through minor trauma. When the sacrum is loaded with the superincumbent weight, the pelvis is symmetrical and the line of gravity is posterior to the transverse acetabular axis, the pelvis has limited motion and the ligaments have a balanced tension. When the line of gravity moves anterior to the transverse acetabular axis in order to lift, bend or lower, or during pregnancy, the sacrotuberous ligament is loosened, the ligamentous balance is disrupted and can result in a dysfunction in anterior rotation of the innominates on the sacrum. The innominates will rotate cephalad and laterally on the sacrum and temporarily fixate. The resultant dysfunction will limit normal movement and function of the SIJ and can result in what appears to be a multifactorial etiology. Manual posterior rotation of the innominates on the sacrum to the balanced position will restore normal function and provide immediate relief of pain. Recurrence is controlled by simple specific corrective exercises. Instability can be corrected by proliferant injections to the long and short posterior sacroiliac ligaments and the pubic symphysis. This is probably the long sought mechanism of idiopathic low back pain syndrome.

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KEYWORDS: biomechanics, dysfunction, gait, low back pain, pathology, sacroiliac joint.

INTRODUCTION

When it comes to idiopathic pain in the low back, we all see essentially the same thing. In 1982 White suggested "It may well be that idiopathic backache will be found to be caused by some condition that is a subtle variation from normal. Otherwise, we probably would have found the cause already. If back pain were caused by a highly unusual condition, then fewer people would suffer from this disorder."[1] It is the purpose of this paper to describe a commonly overlooked, reversible, biomechanical dysfunction of the sacroiliac joint as the mechanics of idiopathic low back pain syndrome and its appropriate management.

ONSET

When standing, the pelvis is symmetrical, the sacrum is loaded and ligamentous tension is in balance. No muscle power is necessary to maintain the position of posterior pelvic rotation. Other than some slight movement in the sacroiliac joint (SIJ) in flexion and extension, there is essentially no motion in the joint.

The most critical support necessary to maintain the balanced sacro-innominate relationship when leaning forward is a strong voluntary contraction by the abdominal muscles. (*See Figure 1.*)[2, 3, 4] The SIJ is stable in posterior rotation, but vulnerable to injury with an anterior innominate rotation.

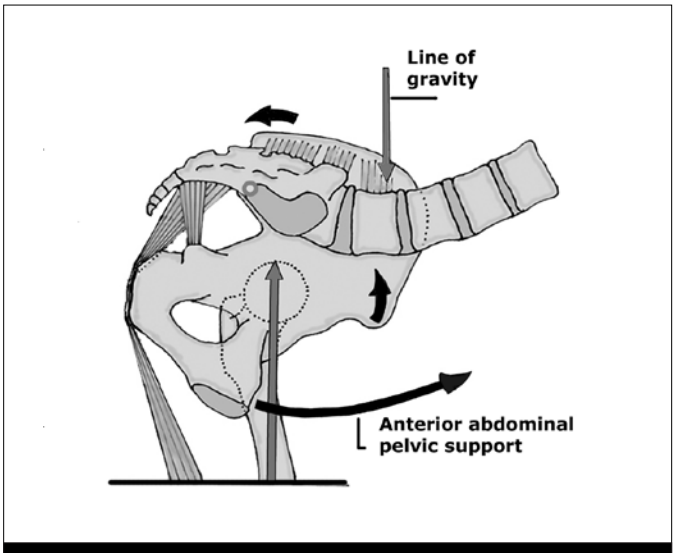

Figure 1. Active abdominal support holds the pelvis in posterior rotation to maintain the ligaments in balance when leaning forward.

If the balanced sacro-innominate relationship is not maintained, when leaning forward to lift, bend or lower, the line of gravity will shift anterior to the acetabula and will cause the innominates to rotate anteriorly on the sacrum on an acetabular axis. The pelvis will also rotate anteriorly with a protruding abdomen or with advanced pregnancy.

DYSFUNCTION OF THE SIJ

Rents in the Joint Capsule: The vertical innominate shear on the sacrum at the PIIS with this dysfunction in anterior rotation may occur with fixation and cause rents in the joint capsule with leakage of contrast media to the lumbosacral plexus, to the root of the fifth lumbar nerve and into the body of the psoas muscle.[5] Cysts may form on the margins of the joint. The long posterior sacroiliac ligament suffers a direct stretch[6], may undergo a visco-elastic failure of the collagen or may become torn or avulsed from its attachment to the PSIS. (*See Figure 2.*)[3, 7]

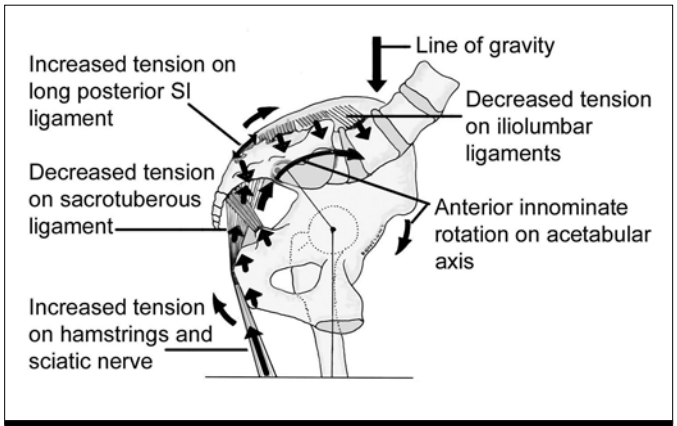

Figure 2. The dysfunction in anterior rotation alters tension in various ligaments.

Ligamentous loosening: The dysfunction in anterior rotation will loosen the iliolumbar ligaments, destabilizing L4, 5-S1 increasing shear and torsion shear to the discs.[8, 9] This is probably the most likely cause of disc disease. Anterior rotation will also loosen the sacrotuberous ligament, destabilizing sacral function and the pelvic diaphragm. The loose iliolumbar ligaments and increase in the lumbosacral angle are precursors of spondylolisthesis.

Primary Painful Points: A sudden release of the balanced position will result in a vertical shear of ilial S3 on the sacral S3 segment at the PIIS. This painful point is always present with SIJD, but it is commonly overlooked. The PIIS is immediately lateral, slightly distal and deep to the PSIS at the juncture between the ilial and the sacral origins of the piriformis and the gluteus maximus. This is the cause of piriformis syndrome. Simply by identifying this primary painful point at the PIIS the practitioner can make a positive diagnosis of dysfunction of the SIJ.

Muscle Separation: The gluteus maximus, piriformis and the iliacus all have origins on the sacrum and the ilia. This vertical shear at the sacral axis stresses these dual origins and causes extra-articular painful points at the PIIS and distal to the PSIS. (*See Figure 3.*) As the sacral origin of the gluteus maximus stabilizes the sacrum when leaning forward, if the innominate bone rotates anteriorly on the sacrum, this muscle separation is enhanced.

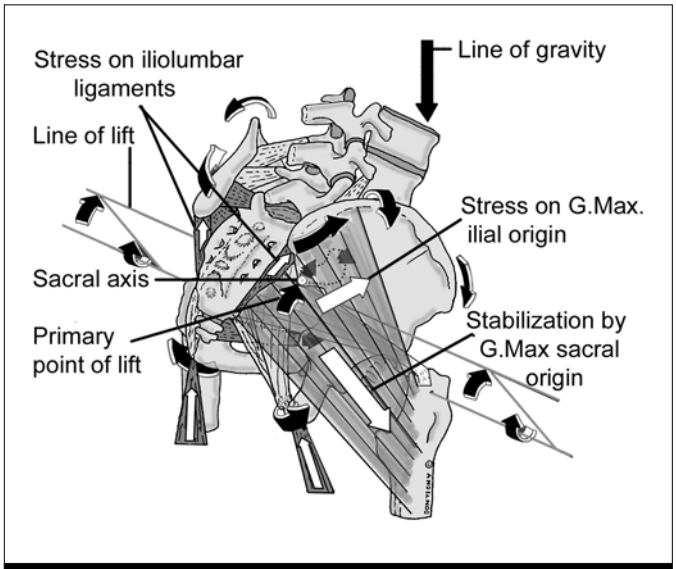

Figure 3. As the sacral origin of the gluteus maximus stabilizes the sacrum, the dysfunction in anterior rotation can cause the ilial origin to separate on a line to the greater trochanter.

The sciatic nerve exits the pelvis just beneath the piriformis and not infrequently penetrates it. Pain and spasm in the piriformis can cause non-disc sciatica.

I remember one 65 year-old woman who's sacral origin of her gluteus maximus was so badly separated from the ilial origin it was palpable and rolled painfully under her ischial tuberosity when she sat. I could do nothing for her and I could not find any physician who believed that she had a dysfunction with her SIJ or a muscle separation. She eventually died without relief. A vertical shearing at the PSIS from the dysfunction on the conjoint origin of the gluteus maximus can cause pain into the trochanter, down the iliotibial band and into the lateral capsule of the knee.

Changes in Leg Length: When the innominates rotate anteriorly they rotate over the acetabula causing the legs to appear longer than previously or, if just on one

side, for the crest to be higher on that side and the pelvis asymmetrical. (*See Figure 4.*) An asymmetrical dysfunction will cause an asymmetrical pelvis with a long leg on one side. A bilateral symmetrical dysfunction will cause both legs to be longer than previously. A dysfunctional SIJ can cause asymmetrical development. *An apparent long leg does not cause pelvic asymmetry. The pelvic asymmetry causes the long leg. The leg length will always shorten with correction and the pelvis will be symmetrical.*

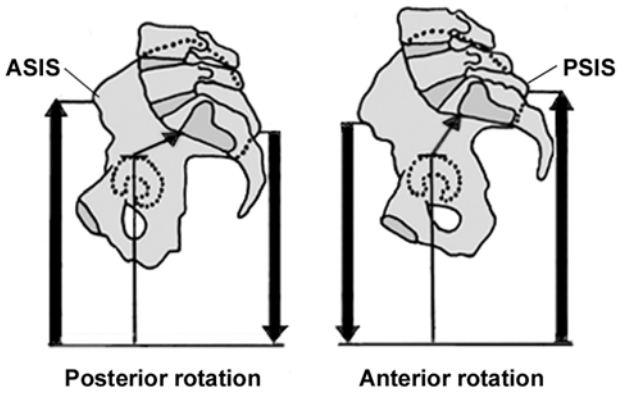

Figure 4. Note the difference in height of both the ASIS and PSIS. Note that with anterior rotation the SIJ moves more above the acetabula causing an apparent long leg. Note also with anterior rotation that the lumbosacral angle is increased, as is shear to the disc.

Some years ago I was doing scoliosis screening for the school system. I noticed a seven year-old boy with a lumbar curve who's mother told me he was scheduled for surgery to be stabilized. He had no complaints of pain, but his pelvis was asymmetrical. I gently corrected an existing dysfunction of the SIJ. Immediately, his pelvis became symmetrical and the lumbar curve straightened. I showed his mother how to correct his pelvis. The problem resolved and the surgery was cancelled.

Muscle and Nerve Stretch: Posteriorly as the innominates rotate up and over the acetabula the ischial tuberosity moves cephalad stretching the biceps femoris and the sciatic nerve. (*See Figure 4.*) This may cause a genu recurvatum or a non-disc sciatic or both. Anteriorly the ASIS move caudad stretching the nerve roots and the iliopsoas muscle. (*See Figure 4.*)[3, 4] Clinical implications of spinal nerve root compression have been well documented[10] and appear to point to disc degeneration as a causative factor.

Similar neurological changes can be caused by a stretch of the spinal nerve roots.[11] Nerve roots are more vulnerable to stretch than peripheral nerves.[11] During elongation the cross-sectional area is reduced with deformity of axons and blood vessels.[11] The elastic limit of nerve roots is reached at 15% elongation when a total mechanical block occurs.[11]

Dorsal root ganglia are more susceptible to stimulation than axons[12]; therefore, sensory changes may be more common than motor defects.

Traction on nerve roots may produce a lancinating pain.[13] Stretching the muscles is counter productive. Correct the SIJ and muscle tension normalizes.

Abdominal Pain: Abdominal pain at Baer's sacroiliac point is not uncommon and the general lack of recognition of this point is responsible for unnecessary abdominal surgery. This point is on a line from the umbilicus to the anterior superior iliac spine, two inches (5cm) from the umbilicus.[14, 15] This point can be found on either side, as opposed to McBurney's appendicitis point, which is two inches from the ASIS and is only on the right. Pain at Baer's point can be relieved immediately with correction[3, 15] or injection into the SIJ.[16] (*See Figure 5.*)

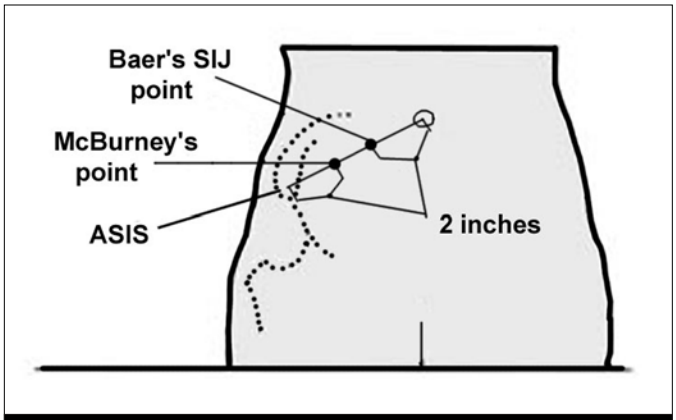

Figure 5. On a line from the umbilicus to the ASIS, Baer's sacroiliac point is two inches from the umbilicus and McBurney's appendicitis point is two inches from the ASIS.

I recall a female patient with a four-year history of low back and abdominal pain. She had both ovaries removed without relief. She was referred to me and was free of both low back and abdominal pain immediately with correction of both of her SIJs. The loss of her ovaries was unnecessary and caused her no paucity of disrespect for her attending physician.

Muscle Inhibition: Dorman found a positional inhibition of the gluteus medius when the innominate is held in anterior rotation.[17] Dananberg found an inhibition of the peroneus longus with SIJD causing a functional hallux limitus.[18] The hip flexors may suffer a positional inhibition when the pelvis is in anterior rotation.

Dysfunctional loading: As the pelvis functions to decrease loading to the femoral head you can expect loading to be increased with dysfunction. This can cause microfractures in the subchondral bone and roughening of the joint surface with eventual arthritic changes. Dysfunctional loading can increase back pain and cause pain up and down the back and legs. Limitation of normal pelvic movement with dysfunction can increase shear and cause instability at the pubic symphysis. When a patient with an arthritic hip has a replacement, in order for the leg length to be equal following surgery, any existing dysfunction should be corrected prior to surgery.

Neck pain: Fukushima found that subluxation of the suboccipital joint provokes severe neck pain and that intra-capsular or pericapsular injection into the SIJ can give immediate relief of neck pain. He recommended that therapy should be initiated to the SIJ dysfunction to relieve neck pain.[19]

Secondary Slippage: Although primary dysfunction is a cephalad and anterior rotation at S3 with S1 rotating caudad, a secondary slippage may occur at S1 and give the appearance of a posterior dysfunction or an upslip with a short leg on the more painful side. *I cannot stress strongly enough that this secondary slippage is clinically insignificant. The dysfunction must be treated as a bilateral anterior rotation of the innominates anteriorly on the sacrum at S3. Correction is only with a manual movement in posterior rotation of the innominates on the sacrum.*

ASSESSMENT

Correction and confirmation: I have found that SIJD is essentially always caused by an anterior rotation of the innominate bones cephalad and laterally on the sacrum with a pathological release of the balanced position. Simply identifying the associated painful points at the PIIS and PSIS can make a diagnosis. These points are extra-articular. An intra-articular injection into the intact capsule will become encapsulated and will reach those points only if there are tears in the capsule.

The AAOS admits to finding a firm diagnosis in low back pain only about 15% of the time.[20] This is probably because their tests are not appropriate to this dysfunction and compels them to miss the diagnosis about 85% of the time. I have not found conventional tests for low back pain to be helpful because they generally have an unsatisfactory inter-rater reliability of only about 25-30%.[21, 22]

Murakami, et al. compared periarticular and intraarticular injections for diagnosis of dysfunction of the sacroiliac joint.[23] Using periarticular injections in 25 consecutive patients with SIJ pain they found that it was effective in all patients. In a comparable group, intraarticular injections were effective in 9 of 25 patients. An additional 16 patients who had no relief from the initial intraarticular injection were all relieved from a periarticular injection.

The improvement rate after periarticular injection was 96% compared to 62% for the intraarticular injection. They concluded that for SIJ pain periarticular injection is more effective and easier to perform than the intraarticular injection and should be tried initially.[22]

Correction is simply the restoration of the position of ligamentous balance by manually rotating each innominate bone so as to cause it to move caudad and medially on the sacrum. This can be done with a traction correction, pulling the leg at about a 45-degree angle of PSLR (*See Figure 6.*); or by a direct rotation, by grasping the innominate and rotating it posteriorly so as to cause the posterior aspect of the innominate to move caudad on the sacrum. (*See Figure 7.*) The patient can be taught to self-correct either with a direct self-corrective stretch (*See Figure 8.*); or with a strong isometric contraction. (*See Figure 9.*)

The leg length will always appear to shorten with correction. With correction, the long leg will get shorter and the short leg will get shorter yet. The joint is very tight and acts similar to a stuck drawer and you must correct one side and then the other, 5-6 times on each side, alternating each time and checking the leg length at the malleoli, not until the legs are equal but until the leg length no longer appears to shorten. Once full correction is obtained the pelvis will be symmetrical, the legs will be of equal length and the patient will be essentially free of pain.

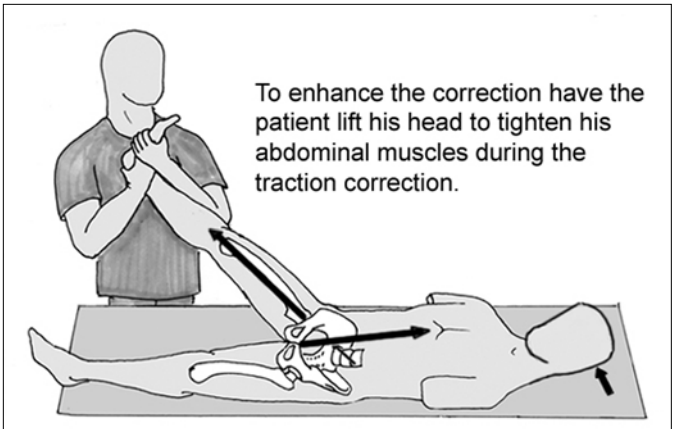

Figure 6. The traction correction. First compare the length of the legs at the malleoli. Stand to one side and gently grasp one foot and ankle and lift the leg as high as comfortable without pain. Put traction on that leg in the long axis. Put that leg down and check the leg length again. You will probably find that leg to be shorter than it was previously. Do the same with the other leg. Continue doing this to each side, one side at a time, alternating legs each time, until the leg length no longer appears to change.

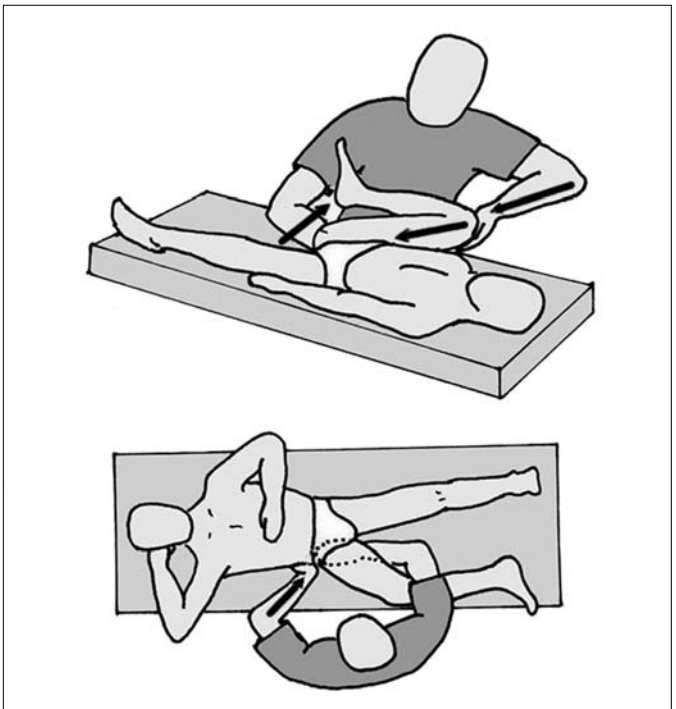

Figure 7. The direct correction. With the patient supine, put one hand under the ischial tuberosity and the other on the posterior aspect of the iliac crest. Now pull up with the underneath hand and push down with the other in such a way as to move the posterior aspect of the innominate caudad and medially on the sacrum.

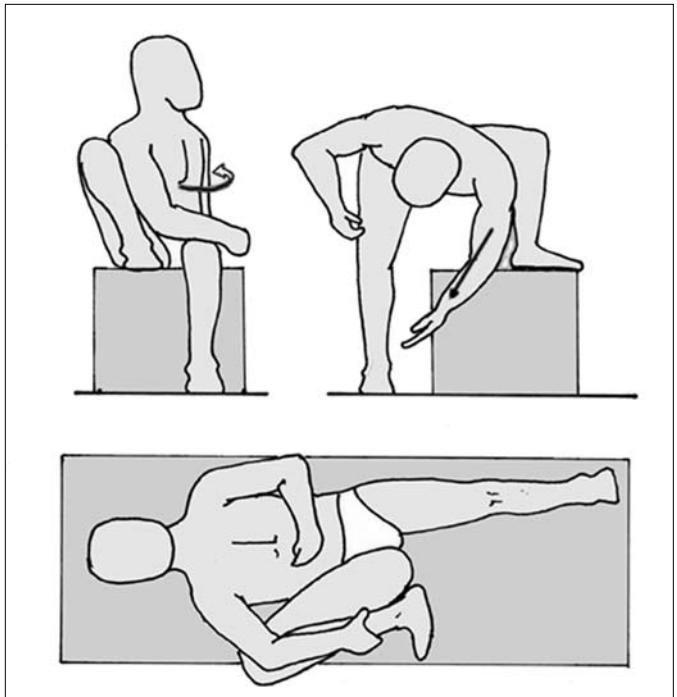

Figure 8. An alternate direct correction. With the patient supine flex the hip and knee so as to bring the knee into the ipsilateral axilla. This can be done in any of several positions.

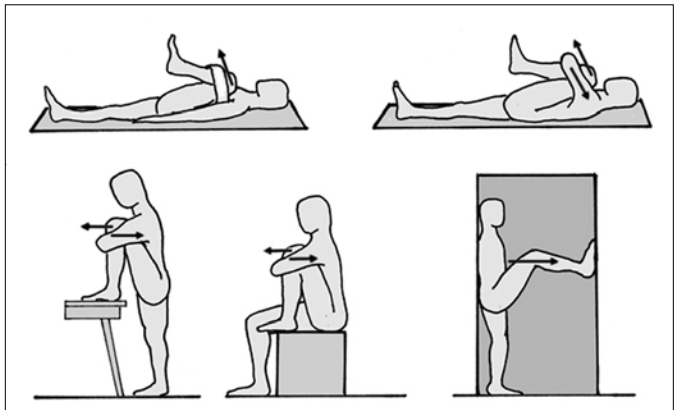

Figure 9. Muscle energy corrections are a very powerful method of correction and can also be done in a variety of positions.

INCIDENCE

In 1928 Yeoman reported that sacroiliac arthritis was responsible for 36% of the cases of sciatica.[24] Davis and Lentle used technetium-99m stannous pyrophosphate bone scanning with quantitative sacroiliac scintigraphy in 50 female patients with ILBPS and found that 22 patients (44%) had sacroiliitis. Eight of these patients (36%)

had unilateral sacroiliitis and 14 (64%) had bilateral sacroiliitis. Of the 22 patients with abnormal scans, 20 had normal radiographs.[25] An outcome study in 1969 of 145 consecutive patients with pain in the low back, 116 or 80% were found to have an anterior rotation dysfunction. Of these, 63 (54.5%) were bilateral. Treatments averaged 5.9 per patient. Relief was frequently dramatic.[26]

In 1992, Shaw reported on 1,000 consecutive cases of low back pain using changes in apparent leg length and movement of the pelvis from asymmetry to symmetry to correctly identify and treat the dysfunction of the sacroiliac joints. He found that 98% of all patients had at least some degree of SIJD and his surgical incidence for herniated discs dropped to 0.2%.[27] Shaw has been ignored. More recently Borowsky and Fagen have suggested that SIJD is far more common than is generally thought.[28]

MANAGEMENT

If the pain is acute I will correct both SIJs, instruct the patient in self-correction and tell them to continue correction every two to three hours all day long for at least three days. The body makes some accommodation to the dysfunctional posture and it takes some time to accommodate to the corrected posture. Correction is always by a manual flexion of the innominates on the sacrum and will cause the PSIS to move caudad and medially on the sacrum. This has been demonstrated on x-ray[2] (*See Figure 10.*) and by measurement.[29]

On the second day I have the patient demonstrate to me how they think I told them to do the corrections. I have found that patients can be quite inventive and may need to be re-instructed. There is no point in doing the corrections improperly. If the patient has no pain by the third day he is discharged to continue with his corrections as necessary.

If the patient has chronic pain I do the same thing for the first three days. I also do some gentle contract/relax stretching as tolerated. If treatment is necessary after ten days I will put them in a lumbosacral support with instructions to put it on when lying supine on the support, doing corrections and then fastening the support. If the support is put on when the patient is erect and uncorrected, the support will only hold them in the uncorrected position. I like the lumbosacral support because of the accompanying instability at L4, 5-S1.

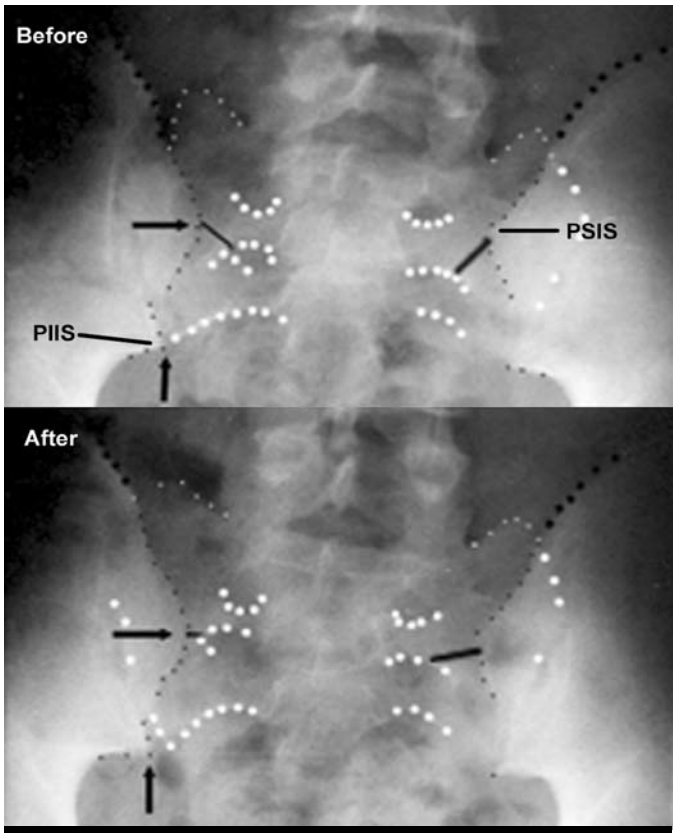

Figure 10. Before and after x-rays demonstrating movement of the PSISs caudad and medially on the sacrum with correction.

Moderate instability responds to Prolotherapy to the long and short posterior sacroiliac ligaments and to the public symphysis if it is unstable. If you use a "shotgun" technique and Prolo all of the ligaments, the joint might tighten in the dysfunctional position, which can be extremely difficult to correct. Similarly, if you Prolo the iliolumbar ligaments before the sacroiliac joints are stable, you might not be able to correct the dysfunction. Prolotherapy may not be effective if the long posterior sacroiliac ligament has been avulsed from the PSIS, or if it is shredded or if it has undergone extreme viscoelastic failure.

I have found that injections of Sarapin are excellent for the relief of trigger point pain along the iliac crests and around the trochanters. This is a non-steroidal, sterile aqueous solution of soluble salts of the volatile bases from Sarraceniaceae (pitcher plant).

Severe joint instability may require surgical fixation, but the joint must be in a corrected position first. Also, if the joint is fixated you will negate its function as a force

couple and loading forces will probably be increased to the femoral head. Forces that cause asymmetry will be blocked posteriorly and transmitted anteriorly to the public symphysis. An attempt to preserve function with a ligamentous repair might prove to be a better option.

I will caution you against the traditional method of manipulation of a dysfunction of the sacroiliac joint whereby the patient is side-lying and the operator pulls back the shoulder and shoves forward and downward on the pelvis strong enough to cause cavitation in the joint. This movement can open the joint at which time the innominate bone may rebound giving you a correction, but there is an inherent danger in this.

Consider, the iliolumbar ligaments are on slack and the lower lumbar discs are vulnerable. The long posterior ligament is on tension and vulnerable. Such manipulation can tear the annulus and extrude disc material as well as avulse or shred the long posterior SI ligament from its attachment to the PSIS causing a chronic instability. Prolotherapy will probably not help this and it may require a ligamentous repair.

CASE STUDIES

Case 1: I was called to radiology where I found a 68 year-old woman with acute pain in the low back and unable to lie flat for an x-ray. She was x-rayed in that position. The right leg appeared shorter, the pelvis was asymmetrical and the right SIJ was not congruent. (*See Figures 11 & 12.*) I then did a gentle correction of both SIJs. Immediately her pelvis became symmetrical, the leg length was equal bilaterally; she was free of pain and discharged.

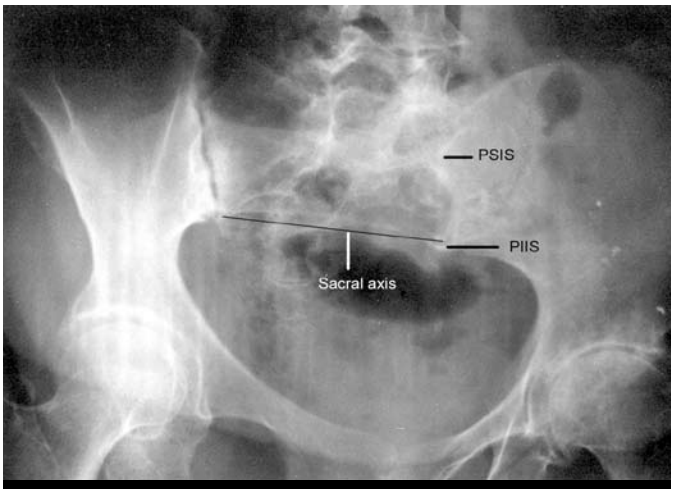

Figure 11. Before correction the patient could not fully lie down. Her pelvis was asymmetrical and the right leg was shorter than the left.

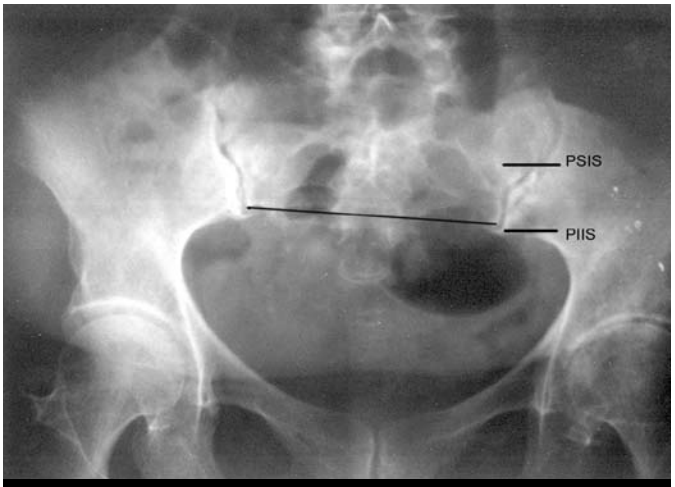

Figure 12. After correction the pelvis was symmetrical; the legs were of equal length and the patient was without pain.

Case 2: A 76 year-old woman with a chronic unstable SIJ for many years. Her husband was able to correct her with excellent relief, however relief was transient. I had advised Prolotherapy some years ago, but none was available in her state. She was finally treated when proliferant injections became available locally. At the first session she had injections of Sarapin to numerous trigger points along the crests and around both trochanters with excellent relief of pain. She had five sessions of Prolotherapy specifically to the long and short posterior sacroiliac ligament, about two to three weeks apart, before she was stable. She continued on her corrective exercise program until that time and now is essentially free of pain.

Case 3: A 23 year-old female injured her low back when she slipped and fell hard on her buttocks while at work on January 23. She was referred for evaluation and treatment on January 24 and was in acute pain. She had no numbness or weakness in the legs and PSLR was negative bilaterally. Changes in apparent leg length demonstrated a bilateral anterior SIJD, worse on the right. Measurements of movement of the PSISs on the sacrum[29] demonstrated a movement inferiorly and medially of 2.5 cm on the right and 1.6 cm on the left with correction. This was a substantial injury and probably involved some tearing of the anterior capsule of the SIJs. She was free of pain following correction, but had a chronic joint instability. She was instructed in a corrective exercise program.

Mobilization of the SIJs to the balanced position always gave excellent relief of pain, but the relief lasted only a few days. A lumbosacral support helped some.

The attending physician referred the patient to a neurologist with these findings in April, who also found involvement of the SIJs on a CAT scan. The neurologist referred the patient to an orthopedic surgeon specializing in sports medicine in May. He told her that she was too flexible to have a serious problem, that her problem was a lack of fitness, that she could become fit simply by riding an exercise bike, and discontinued further physical therapy.

Case 4: A 49 year-old man strained his low back at work on February 3, while lifting a water cooler and was referred for evaluation and treatment on February 7. He stood and walked with his trunk laterally deviated to the right and complained of pain over the right SIJ. This pain was increased with leaning forward, sitting, and coughing or straining. There was no weakness or numbness in either leg. PSLR with the left leg increased pain in the right SIJ, which indicated a possible anterior rotation on the right. PSLR on the right increased the pain on the right side, which indicated a probable clinically insignificant slip at S1 on the right. There was no leg pain with PSLR. Observed changes in apparent leg length with correction demonstrated a bilateral anterior SIJD. The patient was free of pain following correction and instructed in a program of corrective exercises.

He returned on February 8 and was markedly improved and doing his exercises properly. He did well until February 16, when he came in complaining of pain in the left SIJ. He had a high PSIS and a high iliac crest on the left when standing and an apparent long left leg when supine. Flexion of the left innominate on the sacrum equalized the leg length and the patient was again free of pain. Follow-up one month later found him to still be free of pain and continuing his exercises.

Case 5: Email from a chiropractor:

Hello,
I'm not sure if you are still checking these e-mails but I wanted to take a moment and write you on how your very simple sacroiliac movement has ended several years of chronic and severe lower back pain. I fell off a barstool about three years ago and ever since then have had severe pain in my right SI joint that sometimes would radiate down my leg. NSAIDs were the only way for me to get temporary relief. I did approximately 60 spinal decompression treatments because the MRI showed a disc bulge at L5/S1 (the bulge was on the left!). If anything the spinal decompression treatments made me more sore. To say I was desperate would be an understatement. I was under the assumption that my condition was caused by internal disc disease and that the pain was due to the release of chemicals into the surrounding tissue as the disc degenerated. As a chiropractor who also owns a multidisciplinary clinic I tried everything. Friday I was reviewing your website and tried the simple motion several times on each leg while lying on my bed. It seemed the pain decreased. I was sure this was only in my head. Being desperate I continued the exercises several times that day. Saturday I woke up, again with no pain. I put up all my Christmas lights climbing on a ladder all day long, stopping occasionally to do the movement. This is Monday still no pain. I am shocked and in disbelief!

Immediately, today I began teaching your movement to all our patients and to all the doctors that work for me. Could it be that simple? I wonder how many people I have personally misdiagnosed with herniated/bulging discs that really had sacroiliac problems? Since your procedure is noninvasive and puts no torque on a lumbar disc I am implementing it as part of my general protocol for all our lumbar disc patients, as I see it there should be no contraindications in the patient doing this.

Do you have any comments on correlation between the sacroiliac problem and lumbar disc disease? In the past I've done quite a bit of HVLA and honestly believe it can aggravate herniated disc... but your maneuver, I believe, is very safe. I'm not too sure about diagnosing the condition, but honestly what harm does it do to just get the patients doing the movement.

Again thank you. I'm still in disbelief, but I'm very happy to be free of my chronic pain.

COMMENTS

My corrections are not spinal manipulations. There is no high or low speed thrust necessary or desirable. No jerking or popping is expected or sought. This is a precise skill and as with all skills, my method takes some time to learn and to perform. The skilled practitioner can have at least 85-90% of consecutive patients free of pain within about 10-15 minutes.

I rediscovered this dysfunction in 1965. This is what I have found thus far.

I am grateful to Dr. Hauser for this opportunity to present this research on the sacroiliac joint. I hope others will continue and improve on my biomechanics and my method.

For more information and illustrations on the sacroiliac joint, it's function, dysfunction and management. I invite you to visit www.thelowback.com. A CD with over 650 slides and 150 illustrations is also available. If you are interested in a workshop for your group or facility, please contact me. ■

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Office-Based Harvest of Mesenchymal Stem Cells by Tibial Intraosseous Cannulation: Part I

Harry Adelson, ND

ABSTRACT

A recent development in regenerative medicine is the use of bone marrow derived mesenchymal stem cells for the treatment of degenerative musculoskeletal conditions such as osteoarthritis. While the use of autologous stem cells is of immediate interest to all practitioners of regenerative medicine, the complexity and expense of the traditional technique of harvesting bone marrow from the iliac crest with the use of a trocar presents obstacles for Prolotherapists and patients alike. The purpose of this two part article is to propose a novel technique intended to harvest and deliver bone marrow derived mesenchymal stem cells that is at the same time simple, safe, and inexpensive to perform.

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KEYWORDS: bone marrow, mesenchymal stem cells, Prolotherapy, stem cell therapy.

This is the first in a series of two articles investigating novel and inexpensive methods of harvesting and preparing bone marrow derived mesenchymal stem cells (MSC).

Prolotherapy is an alternative therapy for treating musculoskeletal pain that involves injecting an irritant substance into damaged connective tissues to promote the growth of new, healthy tissue.[1] Because Prolotherapy aims to induce the growth of tissues to repair or replace damaged cartilaginous structures, it falls into the category of "Regenerative Medicine".[2] In recent years, many Prolotherapists have begun using platelet rich plasma (PRP) in place of irritant solutions to treat conditions such as osteoarthritis (OA) and tendinopathies.[3] Because of its simplicity, safety, and affordability, PRP preparation and delivery is easily introduced into a Prolotherapy practice. A recent development in regenerative medicine is the use of bone marrow derived mesenchymal stem cells for the treatment of degenerative musculoskeletal conditions such as osteoarthritis. While the use of autologous stem cells is of immediate interest to all practitioners of regenerative medicine, the complexity and expense of the traditional technique of harvesting bone marrow from the iliac crest with the use of a trocar presents obstacles for Prolotherapists and patients alike. The purpose of this article is to describe a novel technique to harvest and deliver bone marrow derived mesenchymal stem cells that is at the same time simple, safe, and inexpensive to perform.

Emerging data supports the percutaneous injection of bone marrow derived mesenchymal stem cells for the regeneration of articular cartilage. Saw, et al. found that postoperative intra-articular injections of autologous bone marrow in combination with hyaluronic acid after subchondral drilling resulted in better cartilage repair in a goat model.[4] Fortier, et al. found that delivery of bone marrow concentrate resulted in healing of acute full-thickness cartilage defects that was superior to healing after microfracture alone in an equine model.[5] Murphy, et al. found that local delivery of autologous MSC to injured joints stimulates regeneration of meniscal tissue in a goat model. In a case study, Centeno, et al. found that autologous MSC culture and percutaneous injection into a knee with symptomatic and radiographic degenerative joint disease resulted in significant cartilage growth, decreased pain, and increased joint mobility.[6]

Prolotherapy[7, 8] and PRP[9] have shown promise in the treatment of OA. The potential benefits of injecting MSC directly into degenerated joints are clear to any Prolotherapist; it could be considered the natural evolution of Prolotherapy. However, bone marrow aspiration has

traditionally been performed in a surgical suite using fluoroscopic guidance with either conscious sedation or general anesthesia making the procedure more complex than most Prolotherapy offices are equipped for. Iliac crest marrow is then concentrated using commercially available systems, rendering bone marrow aspirate concentrate (BMAC), which is then blended with PRP in order to provide the MSC with growth factors to promote growth and engraftment.[10] The complexity of this procedure combined with the expense of the materials makes it cost prohibitive to many patients. Resultantly, this author has sought a method to harvest MSC for reinjection that is safe, simple, and inexpensive.

Intraosseous infusion (IO), a technique for vascular access, was first described in 1922 and was widely used for drug administration in pediatric medicine by the 1940s.[11] Its use declined during the 1950s with the advent of single-use intravenous catheters, but re-emerged in the 1980s[12] and today IO is widely used in emergency medicine both pre-hospital and as an alternative to the central line.[13] A commercially available IO device is the EZ-IO® Intraosseous Infusion System. The EZ-IO is a small, battery-powered, handheld device that drives a beveled, hollow, drill-tipped needle set. It is designed to access the proximal humerus or the proximal or distal tibia. The EZ-IO provides the non-surgeon easy and rapid access to the intramedullary space and enjoys an excellent safety profile.[14]

This past year, this author has injected a blend of autologous bone marrow collected from the tibia using the EZ-IO and PRP into eight large peripheral joints of as many patients as well as into the dermis of the scalp of one patient for the treatment of male pattern baldness and into the dermis of the face of a second patient for the treatment of aging skin. Results are promising and no adverse effects were reported beyond injection discomfort and the initial soreness and stiffness normally associated with Prolotherapy.

To avoid intravascular injection of the high concentration of adipocytes found in long bone marrow, this author has limited this procedure to intra-articular injection of large joints (hip, knee, and shoulder) and superficial cosmetic injections in otherwise healthy patients.

Indications include damaged or degenerated articular surfaces of the shoulder, hip, and knee and damaged cruciate ligaments of the knee. Based on data surrounding blind injection of peripheral joints, ultrasound guidance is used when injecting the hip and shoulder and is optional when injecting the knee.[15] Cosmetic injections to the scalp and face are kept superficial to the hypodermis.

METHOD:

1. Prepare 4mL of PRP with 1mL of anticoagulant citrate dextrose (ACD) in a 10mL syringe (5 out of 10mL of syringe-space is occupied).
2. Identify harvest site—approximately 2cm distal to tibial plateau and 2cm medial to tibial tuberosity.
3. Prepare skin over harvest site.
4. Inject harvest site with 2mL of 2% lidocaine without epinephrine.
5. Position the needle and at a 90-degree angle to the surface of the bone (this will give a slight cephalad orientation due to curvature of the surface bone at this site). (*See Figure 1.*)

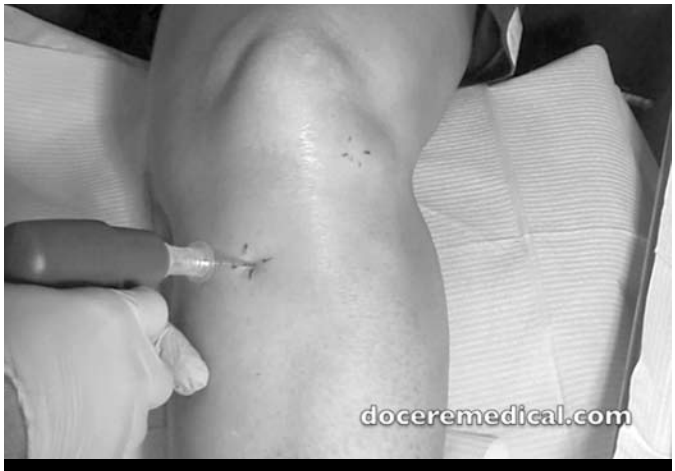

Figure 1. The drill-tipped needle pierces the skin.

6. Advance needle through skin until tip touches bone. (*See Figure 2.*)
7. Squeeze driver's trigger and apply steady downward pressure until a "pop" is felt upon entry into medullary space.
8. Remove power driver and stylet. (*See Figures 3 & 4.*)
9. Attach PRP syringe (with or without EZ-Connect Extension Set) to catheter (if using EZ-Connect Extension Set, flush with ACD prior to use).
10. Draw 5mL of aspirate into a 10mL syringe already containing 5mL of PRP.* (*See Figure 5.*)
11. Remove syringe and/or EZ-Connect Extension Set.
12. Remove catheter by rotating and pulling NOT by rocking or bending.

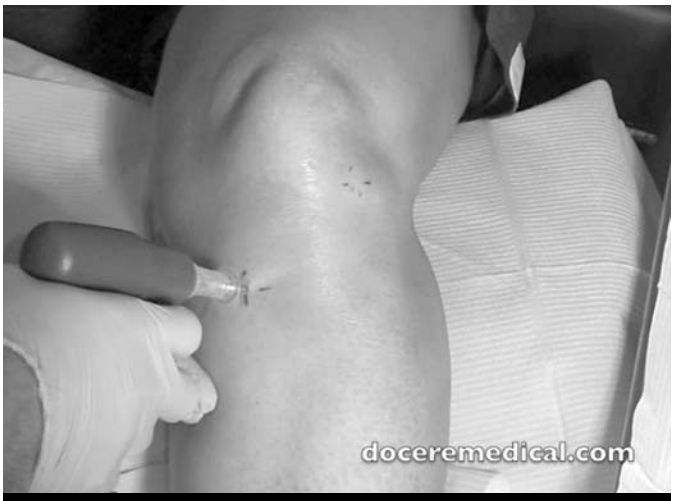

Figure 2. The drill-tipped needle is advanced through the trabeculae into the medulary space.

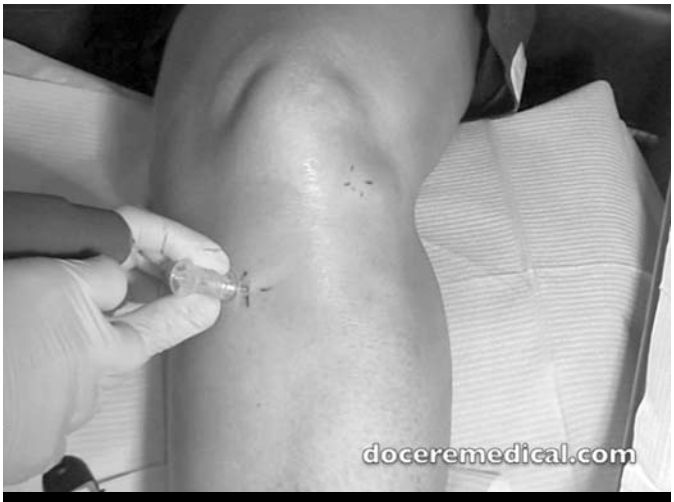

Figure 3. The power driver (drill) is removed.

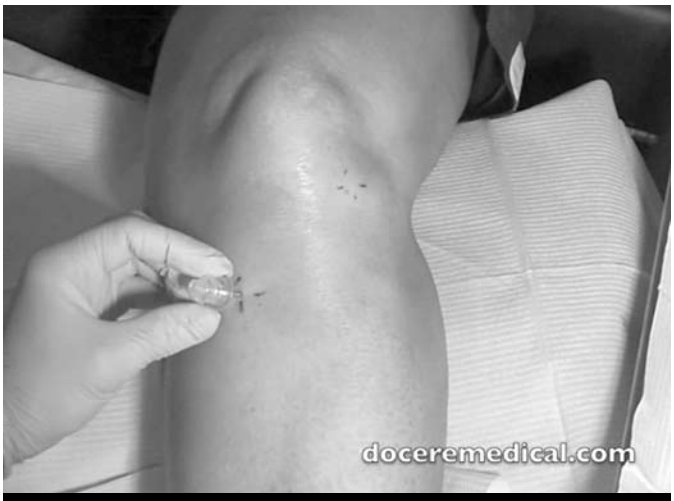

Figure 4. The stylet is removed.

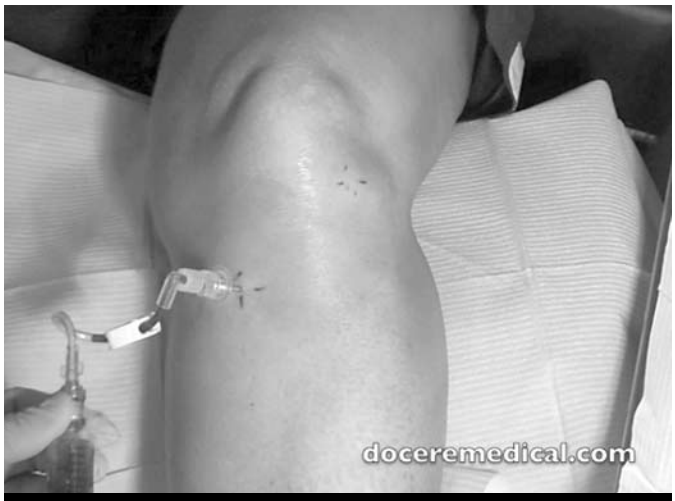

Figure 5. Bone marrow is then aspirated. Typically, 5mL is drawn into a 10mL syringe already containing 5mL of PRP.

13. Apply sterile pressure dressing.
14. Gently mix PRP and bone marrow blend.
15. Prepare skin over injection site.
16. Insert hypodermic needle into joint being treated.
17. Inject 1mL 8% procaine.** (*See Figure 6.*)

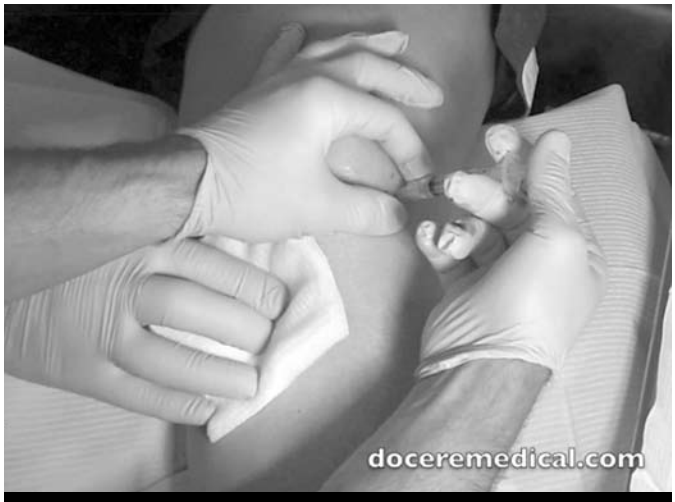

Figure 6. Procaine anesthetic is injected into the joint.

18. Leave needle in place and wait 30 seconds.
19. Attach PRP/bone marrow syringe to needle. (*See Figure 7.*)
20. Inject PRP/bone marrow into joint. (*See Figure 8.*)
21. Remove needle.
22. Have patient remain motionless for 1 hour to allow for cell attachment.†
23. Cephalexin 500mg by mouth twice per day for four days.††

Figure 7. Bone marrow aspirate syringe is attached to the needle hub.

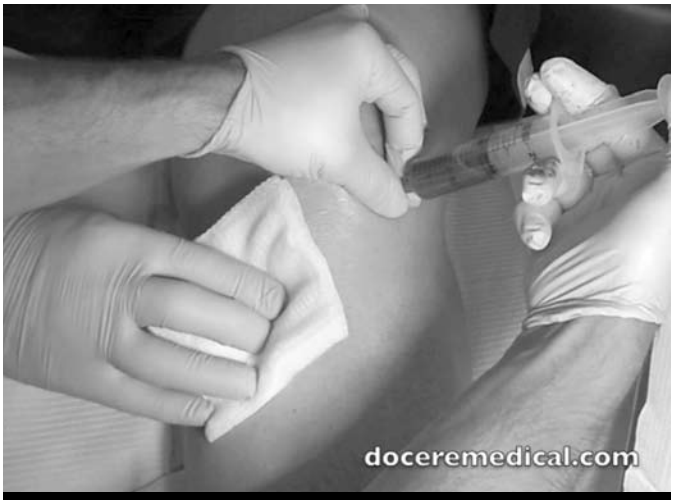

Figure 8. Bone marrow is directly injected into the joint.

* Aspirate over 10mL from a single intrameddulary site is peripheral blood only.

** Procaine is used because of known cytotoxic effects of lidocaine and bupivacaine on synovial tissue[16] and an 8% concentration is used to maximize the effect of a small volume.

† After ten minutes approximately 60% of MSC attach.[17]

†† Common practice among our surgical colleagues is to administer prophylactic antibiotic therapy concomitant with bone marrow aspiration.

DISCUSSION:

This author does not seek to replace the gold standard, BMAC from the iliac crest, with the described method. Rather, because of its technical simplicity and low material expense, tibia aspiration is explored as an alternative treatment for those patients who are candidates for percutaneous injection with autologous MSC and cannot afford BMAC. The described technique is easier and less expensive to perform than is BMAC from the iliac crest, thereby increasing economic feasibility. It is safe; at worst we are diluting PRP with whole blood and adipocytes drawn from the tibia. But does this method of tibia marrow aspiration hold the same promise for clinical effectiveness as BMAC from the iliac crest? The yellow marrow of the tibia contains approximately half the amount of MSC as does the red marrow of the iliac crest.[18, 19] Therefore 10mL of aspirate from a single site in the tibia rather than 60-120mL from up to six sites from in iliac crest, at the very best, is providing approximately 1/12 the number of MSC. How important is concentration and number of MSC? In a clinical case series of sixty patients, Hernigou and his group found percutaneous autologous bone marrow grafting was an effective and safe method for the treatment of an atrophic tibial diaphyseal nonunion. However, its efficacy appears to be related to the number of progenitors in the graft, and the number of progenitors available in bone marrow aspirated from the iliac crest appears to be less than optimal in the absence of concentration.[20]

An obvious improvement on this described method would be to draw a larger volume of tibia marrow and concentrate the MSC with centrifugation. Because of the experimental nature of this procedure, I have not yet felt justified to perform multiple tibia cortical punctures in a single encounter, thereby limiting the aspirate volume to 10mL. My rational for not concentrating tibial marrow at this early stage is because of the uncertainty of how centrifugation would affect delivery of MSC. Tibia marrow has a high volume of adipocytes compared to iliac crest and MSC are highly adherent.[21] Subsequently, there is potential for the MSC to adhere to the adipocytes and thereby be lost during centrifugation. The adherent nature of MSC presents an additional pitfall: the EZ-IO is designed for rapid delivery of emergency medicines and fluids, not for marrow aspiration, and therefore the needle has only a single, large port. This may disallow for the creation of sufficient negative pressure to pull MSC free from the tissue mass. MSC harvest from the tibia could be improved by the creation of a specialized tibia marrow instrument that is longer to allow for repositioning for multiple aspiration sites with a single cortex puncture and includes a multi-port, fenestrated catheter and a Jamshidi-style needle for bone coring. Above all, laboratory investigation into best-

practice tibia marrow MSC preparation is required to determine if tibia marrow aspiration holds promise.

This author seeks to find a safe, simple and affordable method for MSC harvest and presents the concept of tibia marrow collection in its earliest stages in hopes of creating interest among colleagues for collaboration into further investigation. This author welcomes communication from the Prolotherapy and surgical communities.

Please direct communications to harry@docereclinics.com. ■

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FOUR-LEGGED PROLOTHERAPY

Veterinary Case Studies

Babette Gladstein, VMD

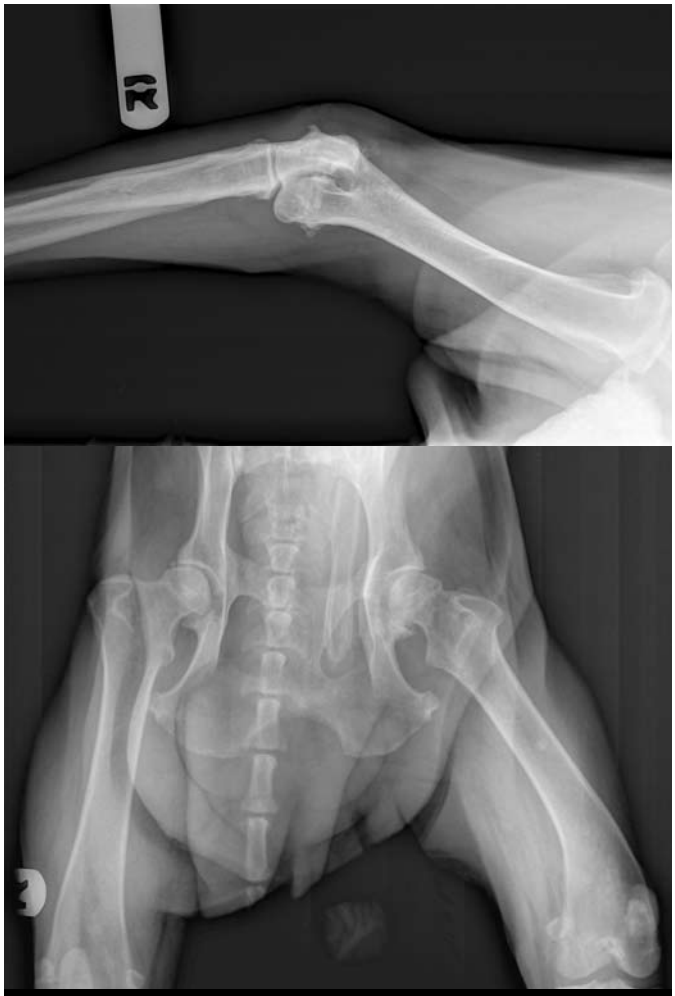
Multi joint Prolotherapy cases are common occurrences in the Canine. Many injuries and pathologies respond extremely well to treatments when several joints are treated verses just the site of primary injury.

OSIRUS - 11 YEAR-OLD MALE NEUTER PIT BULL POLYARTHRITIS, PROLOTHERAPY, AND PIT BULLS

This is not a tongue twister, but a veterinary confirmation challenge. Multi joint arthritis and drug sensitivity are issues not uncommon for the pit bull which make this breed a problematical anomaly to the owners and the veterinarians trying to treat them.

Osirus, an 11 year-old male neuter pit bull, was surrendered to the Humane society in the spring of 2010 after his owner had been relocated. When he was turned in, Osirus had a left partial ACL tear and a classic bilateral hip dysplasia, exhibited more prominently on the left hip. His elbows were exhibiting signs of dysplasia as well. He was not using his left hind leg other than a peg, and had a heavy (3 out of 5) compensatory limp on the right front of his body. On physical exam, he was painful on palpation of all joints, and in his lower back as well. (*See Figures 1 & 2.*)

Osirus, an 11 year-old male neuter pit bull.



Figures 1 & 2. Osirus X-rays read by Van William Knox, VMD, Board Certified Radiologist. Two digital radiographs - a craniocaudal radiograph of the right front limb from the shoulder to the antebrachium, as well as a VD pelvic radiograph that includes the stifles, dated 6/12/10. The right front limb shows elbow joint DJD that involves the lateral and medial humeral epicondyles as well as the ulnar medial coronoid process. An additional bone opacity lesion is seen proximolateral to the olecranon, either lateral to the lateral humeral epicondyle or proximal to the olecranon, that is most likely soft tissue dystrophic mineralization. The pelvic-to-stifles radiograph shows bilateral coxofemoral joint DJD that manifests as irregular and thickened femoral heads and femoral neck osteophyte formation. Spondylosis deformans affects the lumbosacral joint.

We changed his diet, included EFA supplementation (Omega 3 fatty acids), and started (weekly) Adequan injections. We scheduled five Prolotherapy sessions three weeks apart and treated his knees, hips, elbows. By the third session, his gait was back to normal and all feet were

properly bearing weight and placed firmly on the ground. On the sixth session, we included ACell[1] in the protocol. Within 10 days after those injections, Osirus was no longer painful on palpation of hips, knees, or elbows. In the five months since the last treatment, he has gradually improved and no additional Prolotherapy has been needed. Osirus has regained normal mobility and gate. His limping has completely resolved and he is walking, running, and playing like a normal dog. His pain level has dissipated, without the use of drugs. His worst residual issue is a bit of stiffness sitting and standing. Osirus could not stand up on his own prior to his treatments and has now returned to function; age related residual stiffness is merely a trivial affect.

METHODS

We did six Prolotherapy treatments in all. Five were a series of injections of dextrose, lidocaine, vitamin B12, and (Heel's) Traumeel in equal parts. The sixth was a combination treatment of the above, but the right hip and knee were also injected with ACell[1] (5cc). Normal needle size was 1.5-inch by 22 gauge for hip injections, and 1-inch by 25 gauge in and around the knee.

Hip treatments of 5cc were injected at the dorsal and lateral aspect of the hip at four injection sites in and around the articular capsule, surrounding the femoral head of both hips.

Knee treatments of 5cc were injected in and around both knees. Injection sites for the knee: lateral tibial collateral ligament, under the infrapatella bursa, into the tendon of the long digital extensor and deeply into the joint space under the patella ligament. Treatments took place approximately three weeks apart.

Elbow treatments of 3cc were injected in and around the elbow. Injection sites for the elbow: the radial head and the annular ligament, the external condyle of the humerus and articular ligament at the radial head, radial and lateral epicondyle at the lateral collateral ligament and the top of the lateral digital extensor on the lateral aspect of the elbow, and the joint capsule.

CONCLUSION

Polyarthritis and generalized lameness in older animals can be effectively addressed with Prolotherapy. Hips, knees, and elbows can be treated to improve ambulation, diminish pain, and improve overall comfort of the animal without using drugs, such as NSAIDs. Using Acell[1] to complete the Prolotherapy treatments enhances the overall healing of all areas and lengthens the time in between needed follow up visits. ACell[1] also helps with the pain associated with both hip and elbow dysplasia. The cases where I add ACell to the protocol typically need fewer follow up visits for pain.

RUSSEL THE BRUSSELS GRIFFIN - 2½ YEAR-OLD MALE WHEN ACL SURGERIES FALL SHORT - HOW PROLOTHERAPY HELPS TO ALLEVIATE POST SURGICAL LAMENESS

Surrendered to the Humane society with an ACL rupture on the right side, after traditional ACL surgery, Russel refused to place his foot back down. He was presented to me one month post ACL repair, still holding up the leg. On palpation he was painful on the corrected knee as well as both hips. X-rays indicated hip dysplasia and since normal traditional ACL repair is always isolated to fixing the knee, the hip dysplasia and pain needed to be addressed. (*See Figure 3.*) We proceeded with Prolotherapy, five sessions, two weeks apart. I treated the knee and also the hips. After the third session, Russell started bearing weight. During this time, electrical stimulation was administered on either side of the knee to further help reset NMDA (N-methyl-d-aspartate nerve receptors) and drop the chronic pain response. Simple physical therapy techniques were administered to aid the rehabilitation efforts. At the end of 10 weeks, Russel was back to normal and adopted by a new owner who lived in a fifth floor walk up, and Russel continues to do well.

Russel, a 2½ year-old male brussels griffin.

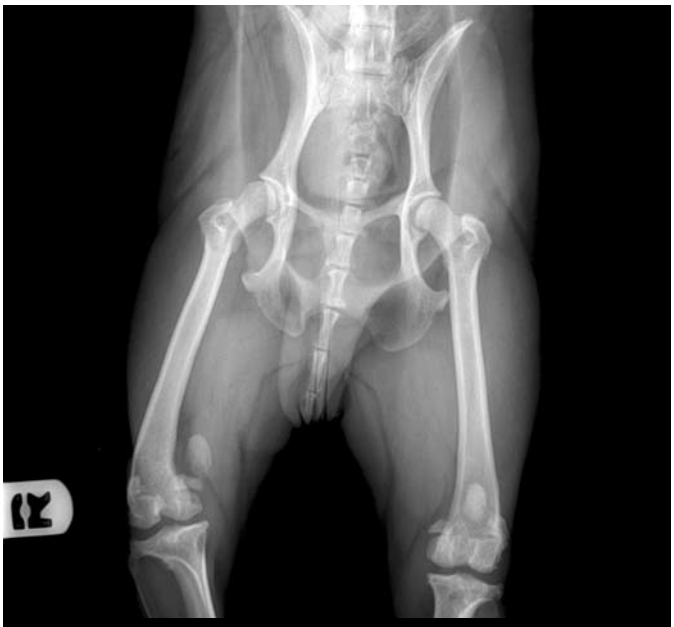


Figure 3. Russel X-ray read by Van William Knox, VMD, Board Certified Radiologist. VD lumbar spine and pelvic digital radiograph, dated 6/29/10. DJD (degenerative joint disease) on the cranial margins of the acetabulae (hip joint) along with apparent subluxation of the right coxofemoral joint. Medially luxated right patella with lateral bowing of the distal right femur.

METHODS

Injections of dextrose, lidocaine, vitamin B12, and (Heel's) Traumeel in equal parts. Hip treatments of approximately 3cc were injected at the dorsal and lateral aspect of the hip at four injection sites in and around the articular capsule surrounding the femoral head, of both hips.

His knee treatments of 3cc were injected in and around both knees. Injection sites for the knee: lateral tibial collateral ligament, under the infrapatella bursa, into the tendon of the long digital extensor and deeply into the joint space under the patella ligament. Treatments took place approximately two weeks apart.

A handheld TENS machine was used at low settings on either side of the surgery knee. With rubber pads and ultrasound gel, handheld for five minutes a day for 30 days.

CONCLUSION

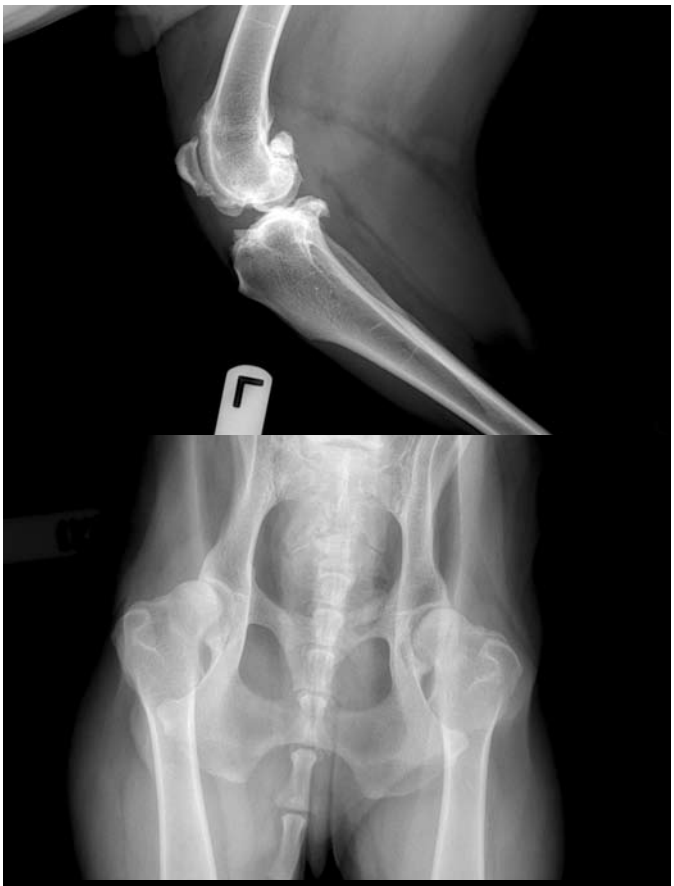
Small breed dogs, less than 20 lb, that do not respond well to traditional ACL surgery, may need and respond well to Prolotherapy for the injured knee. Prolotherapy can also work well in the hips to help them to walk again and have a normal gait. Prolotherapy is helpful in facilitating and accelerating rehabilitation in knee surgery by addressing corresponding hip problems in small breed dogs.

FLOPS - 10 YEAR-OLD MALE NEUTER SHEPHERD MIX

The diagnosis was polyarthritis of the hips and knees. On visual and physical exam, Flops was a healthy and strong dog, weighing about 70 lbs. Flops had been adopted from the Humane society as a six month old puppy, but was returned at 10 years old because the owner lost his home. On a lameness examination, Flops could not sit down —there was pain on palpations over both hips and nearly frozen painful knees. His gait was short and stilted, and stiff. We started him on EFAs and injectable (weekly) Adequan.

The first two sessions of Prolotherapy were to his hips but did not improve his stiffness or his gait. So we proceeded to take full X-rays of hips and knees. Sedation was necessary for the X-rays. (*See Figures 4 & 5.*) While under anesthesia, I administered another session of Prolotherapy. The X-rays showed Flops had hip dysplasia with bone spurs inside of his knees. This was his third Prolotherapy session, and this time both hips and knees were treated. The fourth session consisted of ACell[1] injections in both knees and the worst hip. Although the dog is still a bit stiff, the ACell[1] treatment was the one treatment that helped with the pain in his knees. That session was October 3rd, 2010 and as of December 15th, there is an overall improvement and abatement of clinical signs. He is practicing sit stands daily and is actually able to partially bend his knees. We will monitor this case for any signs of back sliding.

Flops, a 10 year-old male neuter shepherd mix.



Figures 4 & 5. Flops X-rays read by Van William Knox, VMD, Board Certified Radiologist. Lateral digital radiograph of the left stifle, dated 10/3/10. DJD (degenerative joint disease) on the proximal and distal patellar surfaces, trochlear ridges, gastronemius sesamoids, and tibial plateau. Increased joint fluid +/- soft tissue thickening in the cranial compartment of the stifle joint resulting in a loss of the cranial fat pad. VD pelvis-to-stifles digital radiograph dated 10/3/10. Bilateral subluxated coxofemoral joints with bilateral femoral neck thickening, left worse than right. Bilateral and marked stifle DJD. Lateral spondylosis deformans from L5 - L7.

METHODS

Technically, we did four Prolotherapy treatments in all. There were three series of injections of dextrose, lidocaine, vitamin B12, and (Heel's) Traumeel in equal parts. The fourth was a combination treatment of the above but the right hip and both knees were also injected with ACell[1] (5cc). Normal needle size was 1.5-inch by 22 gauge for hip injections and 1-inch by 25 gauge in and around the knee.

Hip treatments of approximately 7cc were injected at the dorsal and lateral aspect of the hip at 4 injection sites in and around the articular capsule, surrounding the femoral head of both hips.

His knee treatments of 5cc were injected in and around both knees. Injection sites for the knee: lateral tibial collateral ligament, under the infrapatella bursa, into the tendon of the long digital extensor and deeply into the joint space under the patella ligament. Treatments took place approximately three weeks apart.

CONCLUSIONS

Prolotherapy is helpful, although not curative, with bone spurs of the knees. It can assist with overall pain levels, and in this case, be supportive of hips and overall arthritis of both the hips and the knees. Combined with ACell[1], this non-surgical solution is a great alternative to long-term functionality of large breed dogs with age-related multiple joint involvement malfunction.

1. ACell's MatriStem™ is a natural three-dimensional extracellular matrix (ECM) which provides an optimal environment for the body to regenerate site specific tissue. The bodies own progenitor stem cells migrate and attach to the MatriStem™ ECM which provides everything cells need to grow and regenerate, including different types of collagens and growth factors. ACell's MatriStem™ products also contain naturally occurring anti-bacterial, anti-inflammatory and analgesic properties which facilitate healing.

SPECIAL THANKS TO VAN WILLIAM KNOX, VMD, BOARD CERTIFIED RADIOLOGIST

Dr. Knox has commented on these and many other of the X-rays previously submitted to the *Journal of Prolotherapy*.

Dr. Knox graduated from Princeton University with an AB in Biology in 1989. He received a VMD from the University of Pennsylvania in 1994 and completed a one year internship (small animal medicine and surgery) at The Animal Medical Center (NY, NY) in 1995, worked in small animal private practice in Maryland and Pennsylvania from 1995–2000, completed a three year residency in radiology from the University of Pennsylvania School of Veterinary Medicine in 2003, and completed a one year staff veterinarian position at the University of Pennsylvania in 2004. He currently practices at Susquehanna and Smoketown Veterinary practices in Lititz, Pennsylvania. Dr. Knox is married with two children, three cats, and one dog. Dr. Knox may be reached at Tel: 717-393-8181 or 717-656-6050. Email: vwk4@comcast.net. ■

TEACHING TECHNIQUES

Prolotherapy of the Arcuate Ligament of the Knee

Ross A. Hauser, MD

While most physicians and lay people know terms such as the anterior cruciate and posterior cruciate signify ligaments of the knee, most are not as familiar with the term arcuate ligament. The arcuate ligament is a Y-shaped condensation of collagen fibers that courses from the fibular head, over the popliteus to insert on the posterior capsule. (*See Figure 1.*) Its medial limb joins the fibers of the oblique ligament and is firmly attached to the musculotendinous junction of the popliteus muscle. It lies just behind the lateral collateral ligament and along with it, provides posterolateral stability to the knee.

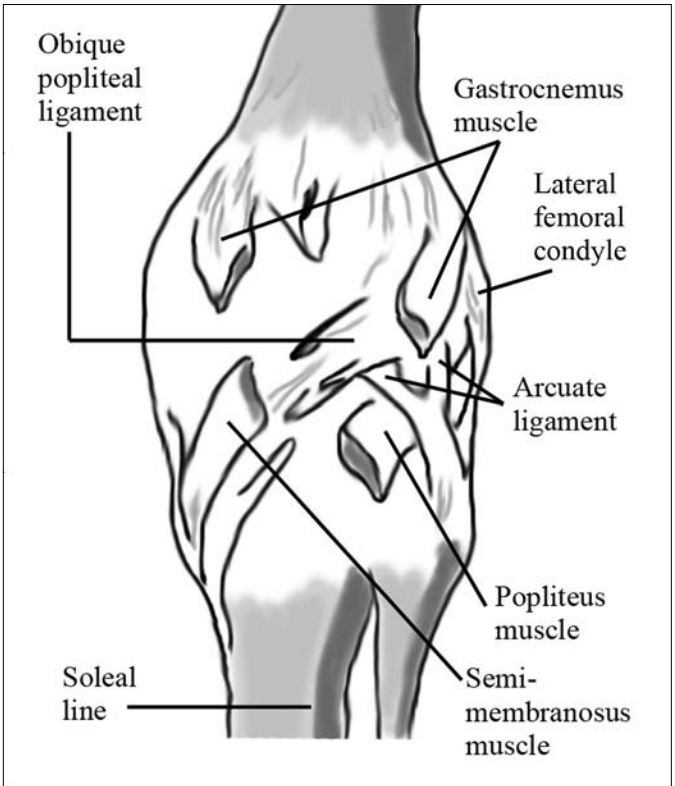


Figure 1. Anatomy of the posterior right knee. The arcuate ligament is one of many structures providing posterolateral stability of the knee.

Any injury or trauma to the lateral side of the knee is likely to injure the posterolateral knee structures. This can occur with a direct blow to a flexed knee while the tibia is externally rotated or a blow to an extended knee with the tibia internally rotated. Rarely is the arcuate ligament injured just by itself. When cruciate ligaments are also injured, typically these are addressed first. In fact, clinically unrecognized posterolateral injury has been suggested as a cause of post-surgical cruciate ligament failure or chronic instability of the knee. Besides physical examination, sometimes MRI is necessary to delineate the extent of the injury.[1] It is important for the Prolotherapy doctor to know about the arcuate ligament because posterolateral rotator instability of the knee is easily missed, misdiagnosed, and mistreated.

CASE STUDY

JH injured her right knee by stepping over a threshold, where she felt her knee go out with pain in the posterior knee. She went to several doctors and was prescribed anti-inflammatories and told to ice the area, which did not offer pain relief. X-rays of her knee were normal. Her prior diagnoses included exacerbation of osteoarthritis, tendonitis of the knee and "strain." Even six weeks of physical therapy did not help and JH noted that it may have made her feel worse. An orthopedic surgeon ordered an MRI of her knee which came back as normal. He administered a cortisone shot which helped JH for a few weeks, but then the pain came back.

Six month after her original injury and after these unsuccessful therapies, JH came to Caring Medical (the author's clinic). She stated that prior to coming to Caring Medical, nobody even examined the back side of her knee. She maintained her primary problem was on the posterior and lateral side of the knee. Besides exhibiting severe tenderness to palpation on the posterior fibular head, she also exhibited a positive posterolateral drawer test. No external rotation recurvatum was present. JH was treated with Prolotherapy to her arcuate ligament complex. She received a total of three monthly treatments to resolve her pain. Before Prolotherapy, her activity was limited to just walking, whereas now she has no limits, as evidenced by a recent pain-free hike up and down several miles of hilly terrain.

PROLOTHERAPY OF THE ARCUATE LIGAMENT

Prolotherapy to the arcuate ligament would involve no more than injecting the proximal and distal attachments of the ligament were it not for the close proximity of the common peroneal nerve. The common peroneal nerve is located on the lateral side of the popliteal fossa where it descends obliquely to become quite superficial along the posterolateral fibula. It then takes a sharp turn around the fibular neck and divides into the superficial and deep peroneal nerves. (*See Figure 2.*) So extra caution must be used with any Prolotherapy treatment along the lateral or posterior part of the knee. Thus, Prolotherapy to the arcuate ligament is done very slowly with great care, in addition to letting the patient know of the risk of peroneal nerve injury during the procedure. If the injection is done very slowly and the nerve is just "tickled" then injury risk is minimized.

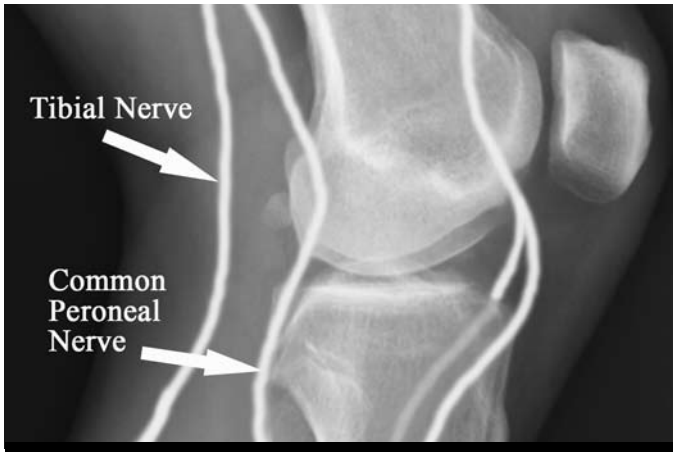


Figure 2. Common peroneal nerve anatomy over an X-ray of the knee. The common peroneal nerve lies very superficial posterior to the fibular head.

In palpating the structures of the posterolateral knee it is important first to mark the location of the posterior fibular head, as this will be the most likely location of the peroneal nerve. First injections are given on the tender area of the arcuate ligament on the lateral condyle of the femur. (*See Figure 3.*) At Caring Medical, I typically start with a 15% dextrose solution with some anesthetic and use a total of 10cc (one syringe) in 4-6 injections in this area. Next, the area around the posterior fibular head is injected with 3-5cc of the same solution with a 25-gauge needle. (*See Figure 4.*) If paresthesias are encountered, they are noted in the chart, with as much description of the location as possible, so in the future, the exact location of the person's peroneal nerve will be noted. Generally,

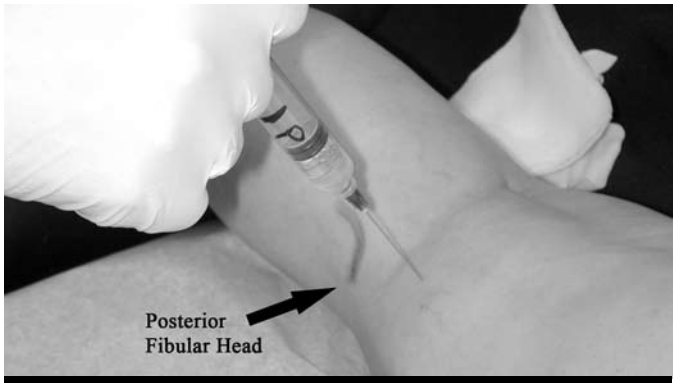


Figure 3. Prolotherapy to the lateral femoral condyle. The superior fibers of the arcuate popliteal and oblique popliteal ligaments attach here. The posterior fibular head is noted because of the location of the common peroneal nerve.

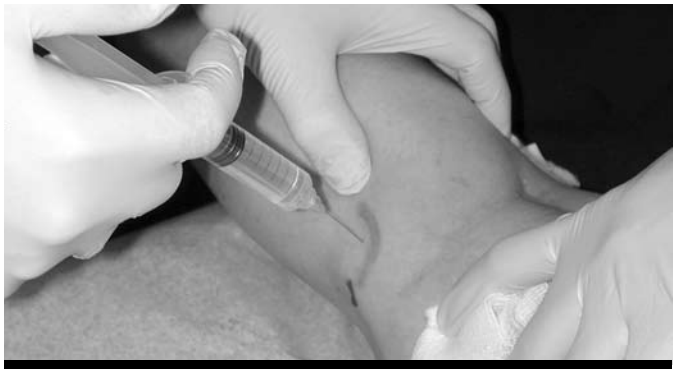


Figure 4. Prolotherapy to the posterior fibular head. These injections are to the attachments on the posterior fibular head of the arcuate ligament complex. These injections must be done slowly because of the proximity of the common peroneal nerve.

patients are seen every four to five weeks and need a total of two to four visits to resolve their pain and symptoms.

SUMMARY

Posterolateral stabilization with Prolotherapy is a good treatment option for patients with arcuate ligament complex injuries. This condition is commonly missed and often occurs with more well known conditions such as anterior cruciate ligament injuries. Prolotherapy to the arcuate ligament and other posterolateral structures must be done slowly and carefully to avoid the common peroneal nerve. Typically, patients need two to four visits to resolve the problem. ■

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IT'S A WIDE WIDE WORLD

Building a Rationale for Evidence-Based Prolotherapy in an Orthopedic Medicine Practice

Part III: A Case Series Report of Chronic Back Pain Associated with Sacroiliac Joint Dysfunction Treated by Prolotherapy - A Six Year Prospective Analysis

Gary B. Clark, MD, MPA

As we delve into what we initially perceive as the truth, It usually becomes "curiouser and curiouser."

Part I of this series discussed the evolution of medical scientific thinking. It visited the historical progression of *Empirical, Deductive, Inductive, and Abductive* reasoning (a suitable acronym being "IDEA"), using a low back pain patient modeled through the ages.[1] Part II discussed the Scientific Method—the classical means to finding "the truth"—using IDEA. It visited application of the Scientific Method for evaluating the practice of Prolotherapy in an Orthopedic Medical Clinic setting. The example hypothesis addressed patients with the same low back pain associated with sacroiliac joint sprain injury.[2]

This, Part III, describes one Orthopedic Medical Clinic's application of logical reasoning (IDEA) and the Scientific Method to the daily diagnosis and treatment of chronic back pain associated with sacroiliac joint sprain injury. The five phases of the Scientific Method (i.e., Question, Hypothesis, Testing, Conclusion, and Reappraisal) easily meld with the five headings of a traditional scientific case study report (i.e., Introduction, Materials and Methods, Results, Discussion, and Conclusion).

Study Introduction

FIRST PHASE OF SCIENTIFIC METHOD: FORMULATE A QUESTION

Step 1.1. *Describe an observation regarding a specific subject of interest.* Seven years ago, the author empirically-abductively noted a seemingly distinct cohort of chronic back pain patients. These individuals predominantly presented with symptoms and signs diagnostic of sacroiliac joint dysfunction (SIJD) secondary to sacroiliac ligament sprain injury.

There already were the empirical-deductive-abductive teachings by George Hackett[3] and his colleagues, the Hackett-Hemwall Foundation, and the American Association of Orthopedic Medicine (AAOM). There also was a large amount of documented basic research on wound healing, which supported the hypothesized theory behind Prolotherapy. Additionally, there had been a few case study and controlled trial reports with mixed results and questionable methodology, which seemed to support the practice—but not irrefutably.[4]

Over that initial year, the author empirically-deductively-abductively treated the aforementioned chronic back pain patients with Prolotherapy of the sacroiliac and iliolumbar ligaments when diagnostically appropriate—based on those largely anecdotal teachings and compelling case study and trial reports. A large share of those patients seemed to respond favorably to Prolotherapy of the sacroiliac joint ligaments with resolution of their back pain symptoms. However, that positive observation was largely experiential and potentially very biased. There was need for more substantial evidence of patient safety, therapeutic effectiveness, and cost-savings in this clinic.

Step 1.2. *Formulate a fundamental question as to the causation of the clinical phenomenon observed.* The above-described observations and practice, as well as premises deduced from the supporting literature and orthopedic medical community wisdom, suggested the following question:

If chronic back pain appears to be commonly associated with sacroiliac joint ligament sprain injury, could Prolotherapy of those joint ligament sprains be significantly procedurally safe, therapeutically effective, and managerially efficient in correcting such sprain injury and resolving patient pain and dysfunction in this clinic?

Study Materials and Methods

SECOND PHASE OF SCIENTIFIC METHOD: FORMULATE A HYPOTHESIS AS AN ANSWER TO THE QUESTION

Step 2.1. *Gather all existing information relevant to the subject issue of inquiry.* He prospectively designed standardized initial intake and ongoing visit recording forms to be used in the following six years. To formulate an empirical-deductive-abductive hypothesis, the author reviewed the current literature. He reviewed all relevant patient records at hand, looking for general patterns and trends.

He prospectively designed standardized intake and ongoing visit recording forms to be used in the following six years. Also, he designed a computerized database to facilitate a quickly accessible, chronological, snapshot follow-up of major independent, dependent, and extraneous variable parameters. All record keeping followed HIPPA rules, maintaining patient anonymity and obtaining patient data use consent.

Step 2.2. *Identify all basic assumptions.* Important to this initial, largely deductive reasoning process, one needs to single out certain basic, important assumptions and preconditions that are premised on already proven truths and established principles as previously outlined in Part II of this series.[2] Generally, these assumptions included managerial and fiscal preconditions, clinical preconditions, and experimental or procedural preconditions.

One of the most important preconditions was that one must gather enough relevant information from a statistically large enough number of individual patient cases on which to deduce, at the most basic level of scientific reasoning, a proper substantiation (or non-substantiation) of the hypothesis. Inductive inferential interpretation through quasi-experimental data analysis might, also, be possible—again, if given enough patient numbers and dependent variables to measure therapeutic effect.

Step 2.3. *Formulate a theoretical hypothesis explaining causation of the observed phenomenon.* The author formulated the following hypothesis for testing:

Prolotherapy is a procedurally safe, therapeutically effective, and managerially efficient therapy for the treatment of sacroiliac joint sprain injury as a healing intervention for the associated chronic back pain in this clinic.

This hypothesis was to be tested prospectively through the course of the next six years of Prolotherapy practice in an Orthopedic Medical clinic setting.

THIRD PHASE OF SCIENTIFIC METHOD: EXPERIMENTALLY TEST THE HYPOTHESIS

Step 3.1. *Identify all of the variables impacting on the testing process*—largely a deductive process.

Independent variables (i.e., what we change therapeutically in order to attempt to create a curative effect) consisted of whatever procedures that would be used for treatment. The treatments under scrutiny included Osteopathic Manual Therapy (OMT), local anesthesia, and Prolotherapy.

OMT: Examining for sacral, pelvic, and lumbar-thoracic alignment and applying appropriate OMT musculoskeletal manipulation were essential for managing all patients through their course of Prolotherapy to minimize their back pain and, also, monitor their reaching the therapeutic endpoint. Examination and manipulation were performed according to a standardized protocol.

Local Anesthesia: Injection of 0.5% procaine, a local anesthetic, was indispensable for its local anesthetic effect to minimize Prolotherapy injection discomfort, as well as being the diluent for the active proliferant substance.

Prolotherapy Anatomic Targets: The specific anatomical target sites that were injected varied. Some patients were treated at just the distal iliolumbar and SIJ ligament attachments, bilaterally, (i.e., omitting injection of the proximal iliolumbar ligaments). Other patients were treated at both the proximal and distal iliolumbar and sacroiliac ligament attachments, bilaterally.

Prolotherapy Proliferants: The various proliferant agents used included 12% Glucose, 1.25% Phenol/12% Glucose/12% Glycerin (P2G), as well as 12% Glucose/12% Glycerin, 0.1% Sodium Morrhuate, 2% Testosterone, and 2% Pumice—these being the concentrations after dilution. All constituents were diluted with 1.0% Procaine resulting in a 0.5% Procaine concentration.

12% Glucose and P2G were utilized as the two basic proliferants. The two terms, 12% Glucose "Plus"

and P2G "Plus," used in this report, refer to various modifications of the two basic proliferants made by adding various combinations of Glucose/Glycerin, Morrhuate, Testosterone, and/or Pumice.

Dependent variables (i.e., what we observe as possibly being affected curatively by the therapeutic change) included measurable subjective and objective clinical and managerial parameters that reflected safety, effectiveness, and cost of the treatments employed. The patients assessed, diagrammed, and gauged their subjective levels of pain—and reported any adverse events. The physician assessed and documented objective, measurable physical examination findings—and documented and followed all adverse events. Patient costs were documented in QuickBooks®.

Controlled variables (i.e., what we maintain as constant or unchanged so as to negate influencing the effect of an independent variable on a dependent variable) included a standardized physical examination and its recording by the physician. Likewise, all treatments were standardized—yet, had to meet the patients' individual complaints and physical findings.

Patient precautions were carefully taught (e.g., to avoid the use of anti-inflammatory medications). These instructions were provided to the patient through a very complete, standardized informed consent form—a copy of which was given to each patient.

Extraneous variables (i.e., an inherent characteristic of the population being studied that might further clarify the independent-dependent variable relationship) included patient gender, age, and right-left hand preference. Also, monitored were assessments of static posture (e.g., shoulder dropping or unleveling, foot arch flattening, and foot-ankle pronation or supination); dynamic posture during gait (e.g., short-leg quick-step and foot-ankle internal rotation-supination); foot-ankle and first toe dorsiflexion strength; Gluteus medius leg abduction strength; leg length comparison; sacroiliac joint mobility; ileal alignment; lumbar, thoracic, and cervical vertebral alignment; and thoraco-costovertebral alignment. Measurements of these ancillary parameters were the product of every musculoskeletal examination and they reflected various forms of associated physical injury and dysfunction.

Step 3.2. *Design an experimental test or clinical protocol that will prove—or disprove—the hypothesis*—largely an empirical-deductive-abductive process.

Patient Selection Criteria: Patients were selected for this case series study if they presented with chronic back pain at any vertebral level and were diagnosed having unstable sacroiliac joint dysfunction. The diagnostic criteria for such symptomatic sacral sprain injury and unstable misalignment were as follows:

- Patient assessment of back pain at any vertebral level in terms of location, severity, and referral or radiation, which the patient documented by diagramming and applying a 10-point Visual Analog Scale (0 = no pain; 10 = most severe pain imaginable)
- Physician assessment of sacral alignment at the sacral inferior angles.

SIJD Diagnostic Criteria for Prolotherapy Candidacy: The physical criteria for the diagnosis of sacroiliac joint sprain injury and unstable sacral dysfunction were assessed with the patient lying on the examination table. Assessment was made of sacral alignment in concert with a complete musculoskeletal examination from plantar arch to nuchal line. If either left or right sacral inferior angle was displaced inferiorly, the criterion for SJID was met.[5, 6] Assessment of several ancillary parameters served to clarify the diagnosis of SIJD and sacroiliac joint stability, including testing *Gluteus medius* abduction strength and assessing lumbar vertebral alignment. The diagnosis was tested by performing OMT to the sacrum, pelvis, and lumbar spine, as appropriate, until the sacrum was normally aligned.

Then, the patient came off the examination table and walked 60 feet to test the patient's sacroiliac joint stability while weight bearing. Upon reassessment on the table, if the sacral inferior angle had returned to its earlier observed inferior displacement, the sacroiliac joint was deemed unstable upon weight bearing and the patient was confirmed a candidate for Prolotherapy.

If the patient remained aligned at the sacral inferior angles, then the sacroiliac joint was deemed stable and the patient was not a candidate for Prolotherapy at that time but was a candidate for watchful follow-up for any eventual sacral misalignment recurrence. The stable patient was followed with other appropriate musculoskeletal therapy such as OMT, Rolfing, and Pilates, for residual musculoskeletal misalignment and imbalance problems—along with normal activity. (*See Figure 1.*)

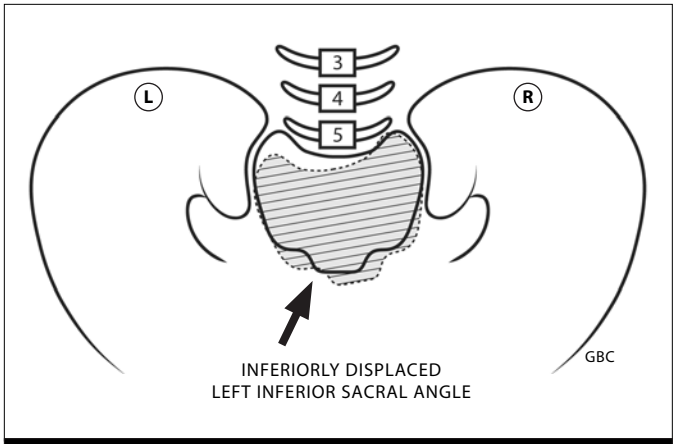

Figure 1. Sacral Misalignment. The left sacral inferior angle is displaced inferiorly as palpated with examiner's two thumbs.

Treatment Criteria: Prolotherapy treatment consisted of a standardized routine of anatomical landmark palpation, identification, and marking; swabbing the injection sites with alcohol and 1% iodine for antisepsis; skin anesthetization with 1% procaine; and performing the Prolotherapy injections. Over the subject six years, Prolotherapy involved a varied selection of anatomical targets and proliferant solutions, depending on the assessed degree of iliolumbar and sacroiliac ligament sprain injury, as described under *independent variables*.

Iliolumbar and sacroiliac ligaments were systematically treated by Prolotherapy bilaterally, requiring three to five injections on each side. 2-4 cc of proliferant were delivered to each injection site using a multiple peppering technique to spread out the proliferant along the targeted ligament attachment. The specific proliferant volumes and sites included 2 cc at each transverse process of the fourth and fifth lumbar vertebrae for the proximal iliolumbar ligament (if included), 4 cc at each anterior-superior iliac crest for the distal iliolumbar ligament, and 4 cc at the interosseous and superficial components of the superior aspect of each sacroiliac ligament. A fifth, 2 cc, injection was delivered to the attachment of the long posterior sacroiliac ligament at each posterior superior iliac spine (PSIS), if it was found to be tender. (*See Figure 2.*)

Treatment was considered at an endpoint when the patient returned to demonstrate a normally aligned sacrum on the examination table after the usual 3-4 week post-therapeutic healing period. The patient contributed an endpoint subjective pain assessment report at that time.

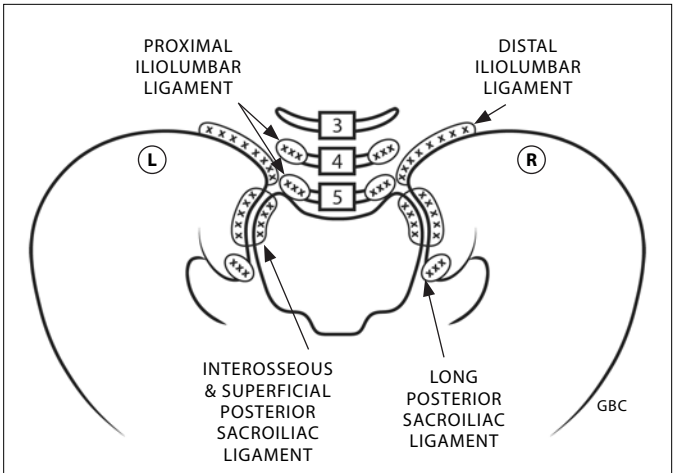

Figure 2. Treatment Injection Sites. Injection sites included the tips of the transverse processes of L4 and L5 (proximal iliolumbar ligament), the superior-anterior surface of the medial iliac crest (distal iliolumbar ligament), the deep interosseous and superficial components of the superior posterior sacroiliac ligament, and the long posterior sacroiliac ligament at the inferior aspect of the PSIS, all bilaterally.

Institutionalizing the Protocol: The uncontrolled, non-randomized clinical trial design was incorporated into all of the formal clinical paperwork and procedures. All procedural and clinical result descriptions were documented in all appropriate patient chart records. Importantly, all parameters were, likewise, documented and tracked using a computer-driven database, as previously described.[2] Each patient received a thorough explanation, aided by skeleton demonstration and hand drawn illustrations of the problem at hand.

Step 3.3. *Perform clinical treatment appropriate to each patient's case to prove or disprove the hypothesis.* This is, perhaps, the hardest step of all the Scientific Method phases. It requires assiduous concentration on completeness of all the standard diagnostic and therapeutic procedures, maintaining consistent detail in all documentation, and pursuing thoughtful follow-up.

Study Results

FOURTH PHASE OF SCIENTIFIC METHOD: FORMULATE A CONCLUSION AS TO WHETHER THE HYPOTHESIS ANSWERS THE QUESTION

Step 4.1. *Collect, collate, and analyze the resultant data.*

General Demographics: Over the course of six years, 77 patients with chronic back pain tested positively for SIJD. Of those, 54 (70%) tested positively for SIJD with sacroiliac instability, meeting the criteria for Prolotherapy candidacy. The other 23 (30%) remained stable after walking 60 feet. Not requiring immediate Prolotherapy, the latter group received musculoskeletal follow-up—there were no known recurrences amongst the stable group.

Of the 54 chronic back pain patients with unstable SIJD, 34 were female (63%) and 20 were male (37%). The female age range was 14 to 68 with an average age of 42.9 years and median age of 44.5. The male age range was 26 to 64 with an average age of 48.2 years. All 54 patients were right-handed. Fifty-two were Caucasian, 1 was African American, and 1 was American Indian.

SIJD Diagnoses: Of the 54 unstable SIJD patients of both genders, 44 (81%) demonstrated a left sacral inferior angle displaced inferiorly, which was diagnostic for a left sacroiliac joint dysfunction. 10 (19%) demonstrated a right sacral inferior angle displaced inferiorly, which was diagnostic for a right sacroiliac joint dysfunction. Of the 34 female unstable SIJD patients, 28 (82%) demonstrated a left sacroiliac joint dysfunction. 6 (18%) demonstrated a right sacroiliac joint dysfunction. Of the 20 male unstable SIJD patients, 16 (80%) demonstrated a left sacroiliac joint dysfunction, while four (20%) demonstrated a right sacroiliac joint dysfunction.

Patients with Left SIJD (LSIJD) and Right SIJD (RSIJD) seemed to present repeated physical patterns. For example, a common pattern of dependent and extraneous variable parameters for a Left SIJD was an inferiorly displaced left sacral inferior angle rotated anteriorly—accompanied by a left-sided quick-step gait; dropped right shoulder; left ileal flexion; restricted left sacroiliac joint mobility; lumbo-vertebral right rotation and left side-bending; thoraco-vertebral right rotation at T12; thoraco-costovertebral left rotation at T6; functionally short left leg; inhibited left leg abduction; supinated left foot; and pronated right foot.

Presenting Pain Patterns and Severity Levels: For the 54 patients, overall, the general pain pattern mirrored that of the two subgroups, 35% complaining of central low back pain and 24% complaining of left low back pain. The combined range of pain was 3 to 9 (out of 10) and the average presenting pain level was 6.1.

For the 34 female patients, overall, the general pain pattern was central (32%) and to the left of center (26%). Their initial presenting pain range was 3 to 9 and the average pain level was 6.8. Among the 28 females diagnostic of LSIJD, there was, also, an overall concentration of pain to the left of center (32%) and central (39%). Their presenting pain range was 3 to 9 and average pain level was 5.6. The 6 females with RSIJD reported a general concentration of pain central (83%). Their presenting pain range was 5 to 9 and average pain level was 8.2.

For the 20 male patients, overall, the general pain pattern was central (50%) and to the left of center (25%). Their presenting pain range was 2 to 9 and the average pain level was 4.8. Of the 16 males with LSIJD, there was, also, a general concentration of pain (50%) central and to left of center (25%). Their presenting pain range was 2 to 9 with an average pain level of 6.8. The 4 males with RSIJD reported a predominance of pain central (50%). Their presenting pain range was 3 to 8 with an average pain level of 5.5.

Prolotherapy Effectiveness: For the 54 patients, overall, the combined average Prolotherapy requirement was 2.9 treatment sessions. The 44 with LSIJD required 3.1 sessions and the 10 with RSIJD required 2.0 sessions.

For the 34 females, the combined average Prolotherapy requirement was 3.9 sessions. The 28 with LSIJD required 3.3 sessions and the 6 with RSIJD required 1.8 sessions. For the 20 males, the combined average requirement was 2.8 sessions. The 16 with LSIJD required 2.9 sessions and the 4 with RSIJD required 2.3 sessions.

Pre- to Post-therapeutic Severity Levels: For the 54 patients, overall, the average change of reported pain, pre- to post-treatment, was a decrease from 6.2 to 1.9 with a percentage decrease of 69%.

The total group of 34 female patients reported an average decrease of pain from 6.1 to 2.0 with a percentage decrease of 67%. The LSIJD group of 28 patients reported a pain decrease by 62%. The 6 females in the RSIJD group reported an 82% decrease. 14 (41%) female patients reported complete pain relief (i.e., zero residual pain).

The total group of 20 male patients reported an average decrease of pain from 6.5 to 1.6 with a percentage decrease of 75%. The LSIJD group of 16 patients reported a

pain decrease by 76%. The 4 males in the RSIJD group reported a 67% decrease. Eleven (55%) male patients reported complete pain relief (i.e., zero residual pain).

Anatomical Target Effectiveness: The "Distal Group" represented the Distal Iliolumbar Ligament and Sacroiliac Ligament, bilaterally. The female and male Distal Group patients required an average of 3.8 and 2.2 sessions, respectively, to reach the anatomical endpoint. Their combined average treatment requirement was 3.3 sessions.

The "Full Group" represented the Proximal and Distal Iliolumbar Ligament and Sacroiliac Ligament, bilaterally. The female and male Full Group patients required an average of 1.9 and 2.6 sessions, respectively. Their combined average requirement was 2.2 sessions. The difference between the Distal Group and Full Group represented a 33% reduction of required treatment sessions for the Full Group.

Proliferant Effectiveness: 12% Glucose, 12% Glucose "Plus", and P2G resulted in reaching the physical endpoint for 20 patients requiring an average of 1.9, 1.5, and 1.7 treatment sessions, respectively—the overall average for all three options was 1.8 sessions. P2G "Plus" combinations required an overall average of 4.0 sessions. Any of the additive combinations to P2G (i.e., any P2G "Plus" combination) caused treatment requirements of an average of 3 or more sessions. That represented an overall 222% additional treatment requirement for the P2G "Plus+" group.

Adverse Events: Review of the 54 records revealed that 2 patients experienced transient numbness, each involving small areas (4 to 9 cm in greatest dimension) over one or the other buttock lateral to a posterior superior iliac spine (PSIS). Both events occurred subsequent to Prolotherapy being injected at the inferior-most PSIS, "Hackett's Point D" landmark. Both patients experienced full recovery without any residual numbness after 2 to 3 months. There were no infections. There were no permanent adverse neurological or vascular events.

Therapy Cost: For 54 patients, the accumulative patient cost for each series of Prolotherapy included $250 for the introductory diagnostic visit (which included diagnostic and therapeutic OMT) and $450 for each Prolotherapy session, which also included OMT assessment and realignment. For the average patient, overall, that amounted to $250 + $1305, totaling $1555, for the resolution of a chronically painful, therapeutically recalcitrant major musculoskeletal misalignment.

Study Discussion

Step 4.2. *Interpret the resultant data*—largely a deductive-inductive-abductive process.

This prospective, unrandomized, uncontrolled case series study report of 54 chronic back pain patients reveals some evidence that helps to characterize Prolotherapy as a safe, effective, and efficient approach for treating chronic back pain secondary to sacroiliac joint (SIJ) ligament sprain injury with SIJ dysfunction. It also raises some questions.

Demographically: The overall numbers were statistically relevantly small. Also, the percentages reflected a self selected statistical "universe"—not a randomized sampling. Accepting that, amongst the 54 total patients, there was a preponderance of female patients; the overall rate for all females (63%) was nearly double that for all males (37%). Additionally, females presented at a younger age. Why? Is this a genomic effect (e.g., general ligament laxity) or a hormonal effect (e.g., relaxin)? Also, there were no left-handed patients.Why? Is SIJD a right-handed disease in a right-handed world? Are left-handed individuals spared the kinetic strain and sprain at their SIJ in a right-handed world? Also, there were no Hispanic patients and only 1 African American and 1 American Indian. Why? Is there a socio-economic or a biomechanical reason?

Diagnostically: The prevalence rates for unstable Left SIJD (an average of 81%) compared to Right SIJD (an average of 19%) suggested a statistical homogeneity between the genders in spite of hormonal differences. However, these figures also suggested that there was a preponderance of Left SIJD in the population studied compared to Right SIJD at about a 4 to 1 ratio. Why? Is this a reflection of SIJD patients being predominantly right-handed and that the left SIJ and its ligaments are continuously at the terminus of the musculoskeletal kinetic chain.[7] As these individuals constantly torque from the left low back into a right-handed world, do they preferentially stress, strain, and sprain the left SIJ ligaments—sparing the right SIJ, which are in the middle of the kinetic chain and protected to some extent?

This report suggests that SIJD is, at least, one significant cause of chronic back pain. It suggests that the physical diagnosis for SIJD can be used for determining therapeutic endpoint. It suggests that a reliable diagnosis of SIJD can be simplified by measuring only one parameter, i.e., sacral inferior angle orientation.

Therapeutically: This report suggests that OMT by itself—without Prolotherapy—may resolve SIJD and its symptoms in, at least, some patients. The computer database created for these patients and chart review showed that OMT resolved the problem in 30% of the patients assessed for Prolotherapy candidacy. The OMT resulted in those patients having a stable SIJ and mitigating their back pain and other secondary compensatory physical dysfunctions. This report does not address how many of those patients may have gone on to have a SIJD recurrence seen by another practitioner—however none returned to this clinic with a recurring complaint although some returned for treatment of other joint injuries.

This report data suggests a therapeutic effectiveness of Prolotherapy for treating SIJD with chronic back pain. It was 100% effective for the 54 patients reviewed—OMT, alone, did not suffice for these patients. The overall number of treatments required was 2.9 sessions. There was a trend that suggested that Right SIJD consistently required fewer treatment sessions (an average of 2.0 sessions for RSIJD versus 3.3 for LSIJD), perhaps reflecting a less severe sprain injury of the Right SIJ ligaments compared to the Left SIJ ligaments in these right-handed patients living in a right-handed world.

Prolotherapy resulted in pain reduction among females, overall, from an average of 8.2 to 1.5 (82%). Males showed an average pain reduction from 5.5 to 1.8 (67%). 41% females and 55% males reported complete pain relief (i.e., zero residual pain), respectively.

Sacral, pelvic, and lumbar misalignment is a complex set of interrelated anatomic and physiological relationships. Resolving just one pain-generating sprain injury and misalignment of the SIJ does not necessarily resolve all the other residual misalignments, skeletal molding, and postural habits that still require further therapy to totally resolve the patient's presenting back pain. There might even be some degenerative disc disease (DDD) and related neurogenic component. However, it is suggested that DDD is much less prevalent a cause of back pain than is conventionally touted compared to sacral, pelvic, and lumbar ligament sprain injury—not one of the 54 subject patients presented with neurological signs.

It might be said that a major weakness of this report is that the treatments varied in terms of the anatomic targets and proliferants used. On the other hand, as a pilot report, these variations provide some internal gauges against which the end results can be measured in a quasi-experimental fashion and generate various suggestions for more specific scientific study. Regarding anatomic target effectiveness, injecting both proximal and distal iliolumbar ligament SIJ ligament attachments, bilaterally in both genders, resulted in an average requirement of 2.2 sessions—as compared to an average requirement of 3.3 sessions when the proximal iliolumbar ligament was omitted. This report suggests that treating the proximal iliolumbar ligament is important in maximizing the effect of this bilateral treatment.

Regarding proliferant effectiveness, this report suggests that 12% Glucose, 12% Glucose "Plus", and P2G proliferants resulted in requiring substantially less treatment sessions than any combination of P2G "Plus." An overall average of 1.8 sessions was required for the first three proliferants, combined, compared to the overall average of 4.0 sessions required for all P2G "Plus" combinations. This report suggests a 222% decrease in effectiveness for P2G "Plus." Why? What is there in P2G "Plus" that may possibly delay healing? Also, the study suggests that Glucose, alone, is as effective a proliferant as any of the other choices. Why? Is there a reason for searching for any more effective a proliferant?

Regarding Procaine effect, injection of a local anesthetic might produce some additional Neural Therapy effect, especially in reducing accompanying lymphedema. This may effect the Prolotherapy effect, one way or the other.

Adverse Events: Two (2) occurrences of transient numbness were the only adverse events. These presumably occurred after needle injury of a cluneal sensory nerve. With 54 patients receiving a minimum of 8 injections requiring an average of 2.9 sessions, the number of total injections amounted to over 1000 Prolotherapy needle wounds. That amounts to an averaged incidence rate of 0.002% per injection. There was no permanent adverse neurological or vascular event. This all occurred in a solo musculoskeletal clinic unassociated with any hospital or organized peer safety committee.

Cost: The average cost of SIJD Prolotherapy in this clinic is $1555. The comparative cost for L5-S1 surgical fusion is $30,000 to $40,000, which often does not resolve pain and dysfunction since the diagnosis of SIJD has been missed. Prolotherapy of SIJD treats the main cause of a many chronic low back pain complaints, some of which are mistaken for L5-S1 degenerative disc disease. Prolotherapy of chronic back pain associated with SIJD is comparatively very cost-effective. Can back surgery boast of such a high cure rate and such minuscule adverse events?

Study Conclusion

Step 4.3. *Draw a conclusion.*

Conclusion: Prolotherapy is an extremely safe and very efficacious (both therapeutically effective and cost-effective) treatment for sacroiliac joint ligament sprain injury causing chronic back pain in this clinic. Furthermore, it raises questions that might be directed to the practice of Prolotherapy in an Orthopedic clinical setting, in general.

FIFTH PHASE OF SCIENTIFIC METHOD: EXERCISE PEER REVIEW TO REAPPRAISE THE OUTCOME RESULTS AND CONCLUSION

Step 5.1. *Distribute the results to other clinicians and researchers.* This published case report is an example.

Step 5.2. *Reobserve, replicate, retest and form a new, refined hypothesis.* I invite all readers of this study to scrutinize this report carefully and critically. I invite all researchers in the field to consider the questions that this report presents. This encouragement is especially aimed at the pursuit of randomized, controlled studies of the overall effectiveness of Prolotherapy for SIJD-associated chronic back pain, as well as more vigorously studying the comparative effectiveness of various anatomic injection targets and proliferant constituents.

This study endeavor has improved the author's design and application of the clinical database, helped to confirm and redirect his personal diagnostic and therapeutic approaches, and hugely expanded his appreciation for the complexity of the human musculoskeletal system—and what we have, yet, to understand, which becomes "curiouser and curiouser."

Part IV, the final installment of this series, will integrate SIJD Prolotherapy with Prolotherapy of the entire weight-bearing musculoskeletal system in an Orthopedic Medical setting—from "plantar arch to nuchal line." ■

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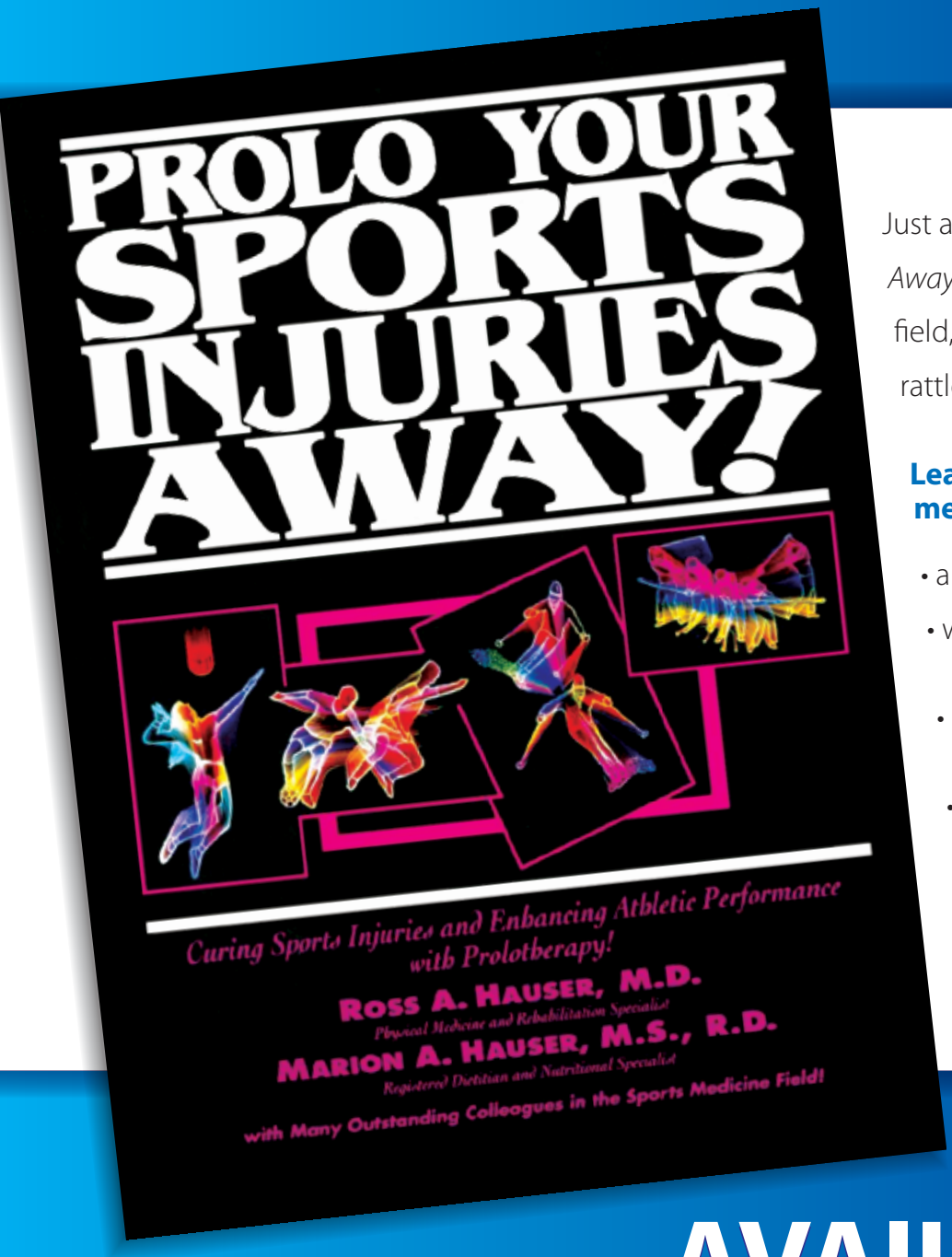

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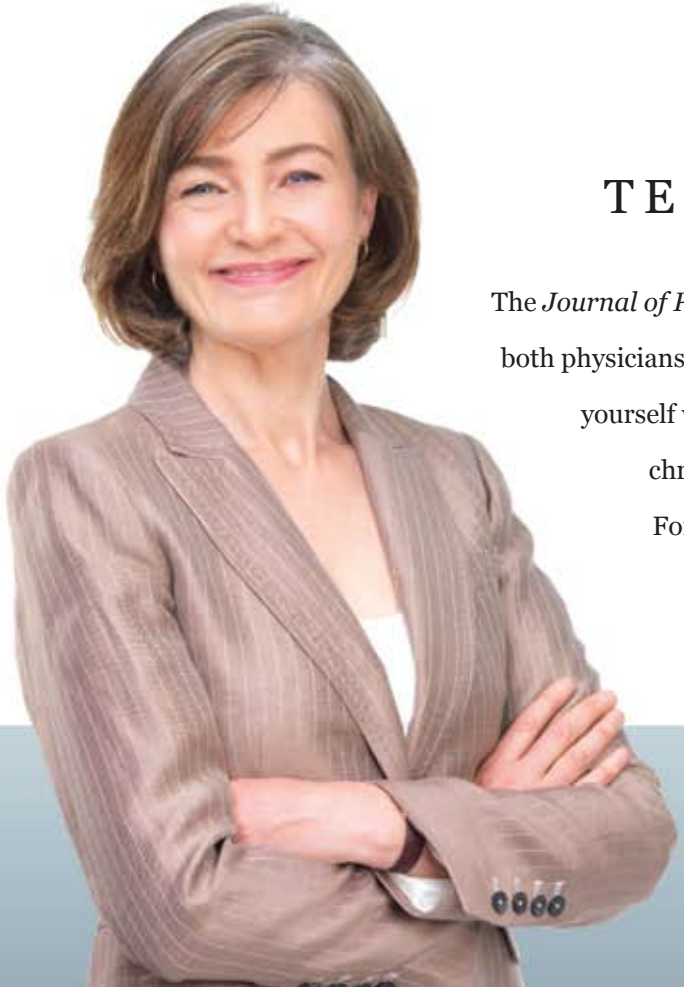

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