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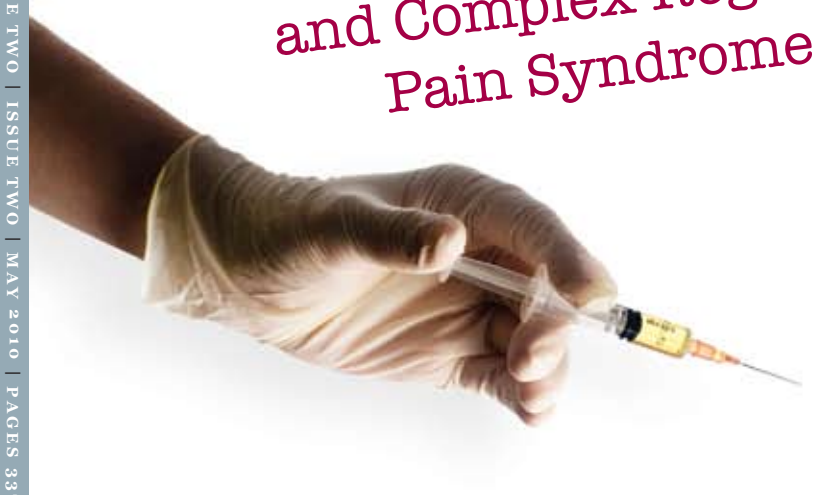
Prolotherapy

Provides Power over Pain for Joint Degeneration and Complex Regional Pain Syndrome



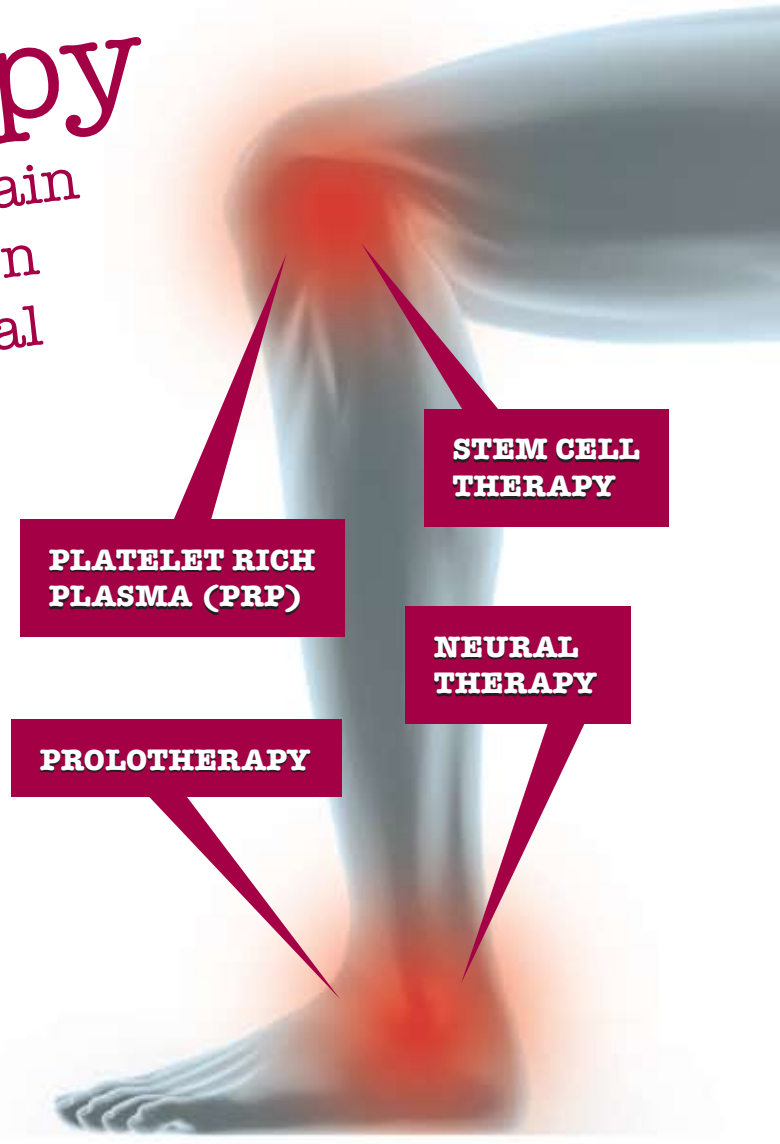


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Table of Contents

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GREAT NEWS CORNER

Prolotherapy Should Be Used in Any Condition that has Ligament Injury as a Cause, Including Reflex Sympathetic Dystrophy

Ross A. Hauser, MD

This issue is loaded with more amazing information discussing some of the more difficult pain conditions that physicians and patients alike often find daunting when trying to help people suffering with them, particularly RSD (or Complex Regional Pain Syndrome). In the words of Michael Rowbotham, MD, renowned expert in the pathophysiology, management, and treatment of neuropathic pain disorders, who wrote a nice review article on RSD, "…no other chronic pain syndrome is as shrouded in confusion and controversy, to the detriment of efforts to rigorously define an evidence based treatment strategy…(as RSD)."[1] Dr. Megan Shields, Prolotherapy physician in California recently wrote me this email:

Dear Ross,

I read with interest the data on the treatment of RSD using prolotherapy. I wanted to let you know that I have had several remarkable successes, as well.

Case #1: *The patient was a concert pianist. After a fractured wrist she developed RSD of the hand and was incapacitated. Over several months I treated the hand with prolotherapy accompanied with physical therapy. She regained full use of her hand and resumed her career.*

Case #2: *The next case involved a woman who had multiple broken bones; feet and legs from a skydiving accident. She narrowly avoided amputation. RSD developed in her feet and ankles. I treated her for a few months and the RSD completely resolved and she regained increased flexibility of the ankle and feet.*

Case #3: *More recently a post-stroke patient developed extensive neurological pain involving all limbs, most predominantly on the right side. She is being treated with prolotherapy on the spine and is improving nicely.*

Case #4: *Also of interest recently, a patient with chronic pain following a hysterectomy has responded well to prolotherapy. After an extensive medical workup and repeated laparoscopic procedures without diagnosis, the patient remained in excruciating pain. I diagnosed her with RSD and began treating the lumbar spine with prolotherapy. After three treatments, the patient is pain free.*

Best, Megan Shields, MD

In 1995, while writing *Prolo Your Pain Away!* I knew conditions such as reflex sympathetic dystrophy had to be included in the book for one simple fact: they responded great to Prolotherapy! Reflex Sympathic Dystrophy (RSD), though currently known as Complex Regional Pain Syndrome, has gone through various name changes throughout the years. The description of the condition by Mitchell and his colleagues, Moorheous and Keen, in their monograph of 1864 remains a true classic:

…sleep is restless, and the constitutional condition, reacting on the wounded limb, exasperates the hyperesthetic state, so that the rattling of a newspaper, a breath of air, another's step across the ward, the vibrations by a military band, or the shock of the feet in walking, give rise to increase of pain. At last the patient grows hysterical, if we may use the only term which covers the facts. He walks carefully, carries the limb tenderly with the sound hand, is tremulous, nervous, and has all kinds of expedients for lessening the pain.[2]

I saw the condition first hand in my residency when our Physical Medicine and Rehabilitation Service was asked to consult on a 12 year-old with the condition. The pain was so excruciating for this youngster that he appeared psychotic. While nerve blocks, pain medications and the physiotherapy provided some temporary relief, they by no means provided a cure. It was then that I started collecting articles on RSD and my interest in chronic pain management was sparked. I continued to follow-up with this person even after I left that service, and it turned out that acupuncture provided him with the greatest relief.

It didn't take long once I started in private practice with Dr. Gustav Hemwall that RSD clients started coming in. I consistently found that a very small amount of pressure would elicit horrible pain, and particularly at the ligament attachments. I also noticed that basically all the patients had long periods of immobility. It then made sense that the reason for their continued RSD was unresolved ligament injury. Fortunately for the patient, I had the cure for it—Prolotherapy! Prolotherapy, along with comprehensive natural medicine, which was sometimes needed, was almost universally successful!

In this issue of the *Journal of Prolotherapy*, it should be clear to the reader that RSD/CRPS is a major chronic pain problem, and to date, there are no clinical trials on the efficacy of various treatments of RSD/CRPS available that use evidence-based-medicine criteria.[3] By the way, the last reference is a quote from a National Institutes of Health workshop! The experience of Megan Shields and myself, along with many other Prolotherapists, is that Prolotherapy is a great adjunctive treatment for RSD/CRPS. It is our hope at *JOP* that this issue will educate both lay persons and physicians that before giving up on treatments for RSD/CRPS, Prolotherapy should be considered.

Generally the by the time someone finds out about Prolotherapy, their pain situation is pretty severe. The typical person going to a Prolotherapist has seen four or five physicians, tried numerous treatments, had a surgery or two, as well as numerous MRI's and X-rays, and have started to lose hope. Then they come across Prolotherapy. For many of these people Prolotherapy will indeed be the answer they have been looking for. Of course, there are times where *in addition to Prolotherapy other methods or therapies are needed*. Surely the more complicated the pain situation – the more comprehensive the care will need to be in addition to basic Prolotherapy. Many articles in this issue discuss how Prolotherapy is used as part of a comprehensive program for pain relief. One such therapy used very often with Prolotherapy is neural therapy, which Gerald Harris, DO very nicely illustrates in his article. Thanks, Dr. Harris, for the work you do to educate patients and doctors on the autonomic nervous system and how neural therapy and Prolotherapy can be so successfully utilized!

Kristin Tate, MD and David Crane, MD contribute a piece they have co-authored reviewing the science and literature of Platelet Rich Plasma grafts in musculoskeletal medicine. Thank you for sharing your expertise in this field with the *JOP* audience! Also, for those interested in PRP and stem cell research, you will want to read the interview with Nathan Wei, MD, who is working hard to further research in stem cell Prolotherapy and proving it can cause articular cartilage to regenerate.

JOP appreciates the work of our regular columnists, Gary Clark, MD and in the veterinarian arena, Babette Gladstein, VMD. Dr. Clark's literature review column takes a look at Baker's cysts, and the use of Prolotherapy for this more unusual type of knee pain case. Dr. Gladstein details five inspiring canine cases with hip dysplasia and how Prolotherapy can help these older dogs get back to their old tricks! Also, the returning author team of Dr. Ann Auburn, DO, Scott Benjamin, PT, DScPT, and Roy Bechtel, PT, PhD demonstrate alternative positioning for iliolumbar injections in *Teaching Techniques*.

From Germany, *JOP* board member, Gunter Baehnisch, MD speaks to those doctors who are new to learning Prolotherapy. He shares his advice on how to begin implementing Prolotherapy in your practice. Another *JOP* board member, Robert Banner, MD, from London, Ontario pairs with physiotherapist, Rob Werstine, PT, to present an interesting case on grade I retrolisthesis and their combined approach to get a patient, Freddie Smith, his life back. Freddie also shares his first-hand story from the patient's perspective.

In addition to Freddie's story, Jane Meyers, OT shares her personal case study, recounting her journey from a life of full-time fibromyalgia pain to becoming pain free. Thank you to both of you for sharing your *Remarkable Recoveries* with us!

Thank you to all of our readers and authors for continuing to promote Prolotherapy! ■

Until the next injection,

Ross A. Hauser, MD

1. Rowbotham MC. Pharmacologic management of complex regional pain syndrome. *Clinical Journal of Pain*. 2006;22:425-429.
2. Shumacker HB. A personal overview of causalgia and other reflex dystrophies. *Annals of Surgery.* 1985;201:278-289.
3. Baron R. National institutes of health workshop: Reflex sympathetic dystrophy/complex regional pain syndromes-state-of-the-science. *Anehsthetisia and Analgesia*. 2002;95:1812-1816.

IN THE SPOTLIGHT

Researching the Regeneration of Articular Cartilage with Stem Cell Prolotherapy: An Interview with Nathan Wei, MD

Ross A. Hauser, MD & Nathan Wei, MD

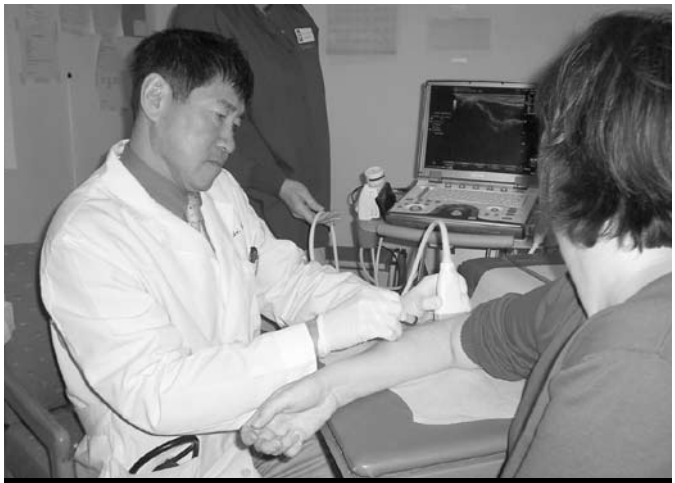
Hauser: Dr. Wei, can you tell us a little bit about your educational background and why you became interested in pain management, and subsequently Prolotherapy?

Wei: I got to this rather circuitously. Originally, out of medical school, I went to medical school in Philadelphia, at Jefferson Medical. I did my residency at University of Michigan and started out in radiology, and switched back to internal medicine. When I was done I had no idea what I wanted to do. I decided to go to the National Institutes of Health and do a two year fellowship. It just so happens that I matched with the arthritis division there. When I was done with my two years there, I still didn't know what I wanted to do. But I was eligible to take the board exams, so I took it, passed. I thought *well, you know, this is it.*

In looking back at it, a lot of fate was involved, because within a few years of starting practice, one of my sisters came down with rheumatoid arthritis. Subsequently, one of my children came down with a form of juvenile arthritis. I guess really when you look at it, I was destined to do this.

Now, the problem with conventional rheumatology training programs is that they do a pretty good job teaching us about the science of arthritis, and how to use very potent drugs to treat arthritis. But they don't really prepare us for what we'll see in private practice. And the types of things we see in private practice are common things, mostly osteoarthritis as well as rheumatoid arthritis, and these types of conditions require a much different set of tools. I've always been very procedurally oriented. I have been an arthroscopist for close to 20 years. I am the only rheumatologist elected to the Arthroscopy Association of North America. Some of the best arthroscopists in the world belong to that (society). So, in terms of using procedures to help patients feel better, that's really where I feel my strengths lie. So, with arthroscopy we've been able to do interventions that help relieve various discomforts related to arthritis.

But more recently, within the last, I'd say three years, I've become very interested in other imaging techniques. Remember, I first started out in radiology. One of those modalities is diagnostic ultrasound. I got hooked up with Dr. Tom Clark, one of the foremost musculoskeletal ultrasonographers in the world, and he introduced me to the use of ultrasound to guide interventions. Along the way, he asked if I ever heard about Prolotherapy. I told him that I didn't really know much about it. I had heard the term, but I didn't even know what it was. So he said he would introduce me to a colleague of his. At a course, he introduced me to Dr. Dean Reeves. Dean, a very nice man, gave me the ins and outs of Prolotherapy and he knew already that I was doing PRP treatments for patients with various tendinopathies and arthritis disorders, and also doing stem cells. He said, "What you are doing right now is a type of Prolotherapy." And so my eyes were really opened at that.



Dr. Wei treating a patient for lateral epicondylitis at his clinic, Arthritis and Osteoporosis Center of Maryland.

Hauser: Dr. Wei, describe for our readers PRP and then stem cell therapies.

Wei: PRP, which stands for Platelet Rich Plasma, is a derivative of whole blood. In other words, what we do is draw a sample of blood from the patient, then we spin that sample down to get small amount of plasma that has a lot of platelets in it. Platelets are components of blood that contain a lot of growth and healing factors. When they go to an area of new injury, these growth and healing factors stimulate the healing response. They accelerate it and send it into work drive. So for certain conditions such as ligament injuries and tendon injuries, where we know that the problem is not really inflammation…but injury, it works to help the healing. I want to emphasize the term tendonitis should not be used. It's actually tendinopathy because the pain associated with tendon problems is related to wear and tear, and not inflammation. So, by guiding the injection of this substance called PRP, platelet rich plasma, into the area where the tendon or ligament is injured, you can actually accelerate, speed up, the healing process. Now that's one part of this whole deal.

The other, what I consider actually an even more interesting aspect, is the use of what are called mesenchymal stem cells. Mesenchymal stem cells are really baby cells. They are cells that have not really differentiated yet. They have not become any specific organ. They are just sort of sitting there waiting to be prompted and stimulated to become whatever tissue you want them to become. If you take a stem cell and give it the right environment, it will become a heart cell, a lung cell, etc. Or in the conditions that we want to treat, it can become a cartilage cell. So what we have been able to do and accomplish is take people with osteoarthritis (wear and tear arthritis, the most common type of arthritis effecting the hip, the knee, and other areas), and by introducing the stem cells, along with an environment that is conducive to their growth and multiplication, we have actually been able to stimulate cartilage growth. And that is exciting because one of the most common surgeries performed in the United States these days is joint replacement. So if we can find a procedure that can prevent or possibly delay indefinitely the need for that kind of surgery, I think that is wonderful.

Hauser: Can you explain where stem cells come from? Explain the procedure in your office.

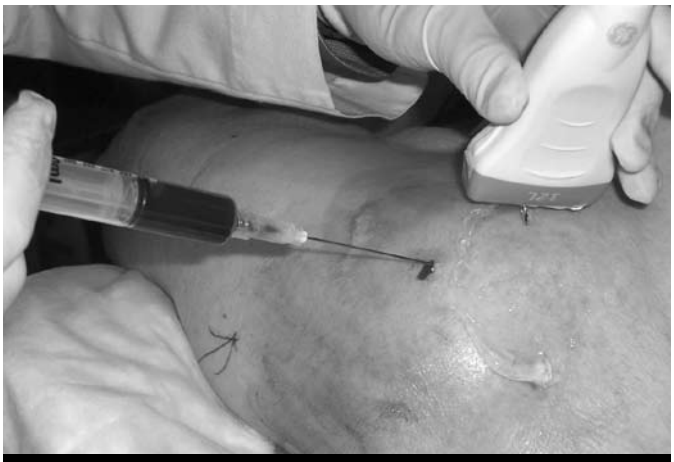
Wei: Fortunately stem cells are present in all of us. They are actually located in the bone marrow. By going to the back of the hip, there is an area called the iliac crest, which is rich in bone marrow. By using local anesthetic and ultrasound guidance, we can actually harvest stem cells, harvest bone marrow from the iliac crest, then prepare it and concentrate a large amount of stem cells, 1.5 million, from this bone marrow aspirate. Believe it or not, this really doesn't hurt.

Hauser: What conditions does stem cell therapy work well for?

Wei: The types of things we see in our office, and again, remember I am a rheumatologist, an arthritis specialist, are osteoarthritis primarily of the hip and the knee. We are looking at other joints as well. Also (we are using it) for patients who have osteoarthritis in the shoulder and who have rotator cuff problems in the shoulder because stem cells can help heal partial tears in the rotator cuff. We have had quite a bit of success with that as well.

Hauser: You are doing a study with stem cell therapy, correct?

Wei: Yes, we are doing a study in order to get around this whole mystique. A whole lot is written about stem cells. If you go to a source like Google for instance, you get a lot of misinformation. Number one, people don't know what stem cells are, and number two, when they're told things, they're told this is the next best thing since sliced bread. They are just not true. What we are doing is taking a select group of patients who range in age from about 25-75. We made that age cut off because we know stem cells in older patients respond less well to stimulus than those coming from younger patients. What we are looking at is osteoarthritis of the knee and we are measuring different parameters, including what is called the Visual Analog Scale (VAS), which is basically what a patient tells us is happening as far as are they feeling better or worse. That is coming from the patient perspective, as well as the physician perspective. We are having patients fill out a WOMAC questionnaire, which is a standard questionnaire used in osteoarthritis studies to describe a patient's ability to perform activities of daily living (ADL's). We measure the speed of a 50 ft walk. Finally, and most importantly in order to create objective data, we are measuring the thickness of cartilage growth in the knee joint, between the knee cap and the upper leg bone.



Dr. Wei performing a PRP injection procedure, under ultrasound guidance, on a patient.

This is called the patellofemoral joint. It is the only joint that is really accessible to ultrasound measurement. We have been able to demonstrate, over a one year period of time, significant improvement in cartilage thickness in most of our patients. Not all. We have had a couple patients not respond and that is to be expected. If you see a paper, and they report 100% success, there is something wrong. I mean there is no treatment in the world that works 100% of the time. The same thing is true with stem cells. But the data that we are getting, both subjective as well as objective, is very encouraging.

Hauser: How many treatments do patients receive and how frequent are the treatments given in the study and in your private patients?

Wei: They only require one treatment. We are only doing one treatment, because we want to see what that effect is. Now, in the future we might learn the patient may require another treatment in order to get better results. The patient may not need one for five years, or may not need another one for 10 years. Because we are at the very beginning stages of this whole stem cell frontier, it is difficult to know what the best approach is.

Hauser: From doing searches on the web, I would say the average patient who goes to a private practitioner generally has the notion that cartilage cells cannot reproduce, or that cartilage thickness cannot improve. Most patients are under the impression that cartilage cells cannot replicate, so if you have degenerative osteoarthritis, you are always going to have it and just wait for a knee replacement. What would you say to that?

Wei: (laughs) That is the kind of opinion and notion we are trying to hopefully change. Because you are right, that has been pretty much the mindset and the message given to patients when they see either their primary care providers or orthopedists—that the cartilage is gone, bide your time and we will replace your joint. The thing is, if the patient still has viable cartilage left, meaning that it is living, that there is still some there, and there is hope that the cartilage can be prompted to grow. That is the promise of stem cells. The best approach for using stem cells in a situation like this, we are still searching for.

A really, really fine stem cell scientist at University of Pittsburgh, Dr. Rocky Tuan, is working with what is called nanofibers. He is doing animal models. These nanofibers provide a really nice framework for stem cells to stick to and help growth. We are also using a matrix as well. I think one of the big problems is people who try to do stem cell therapy, often times just think it is just injecting stem cells into the joint. Far from it. Because cartilage does not have nerves and that is why just the process of wear and tear of cartilage should not cause pain. The pain is actually coming from irritation of the joint capsule. Every joint is a capsule, it is lined by what is called synovial tissue. The pain from osteoarthritis is due to irritation of this capsule and that can come about for a lot of different reasons. But when you treat somebody with stem cell therapy for osteoarthritis, you need to treat the entire region. Not just stick stem cells inside the joint. In addition, you need to give the stem cells some bulk, some framework to stick to so they are not just crushed and washed out of the way with joint movement. There are not only techniques that we are exploring right now, we are constantly improving the process. But I think in a few years this whole approach is going to get better and better.

Hauser: Do you have a post PRP Prolotherapy or stem cell Prolotherapy protocol that you have patients follow? Do you have patients resume normal activity and/or begin special exercises, range of motion, or anything?

Wei: Absolutely. Following a stem cell procedure, or a PRP procedure for that matter, it is important that the patient initially rest for a few days. Then after that, we begin the patient with a graded program of progressive stretching and strengthening of the affected area, trying to avoid any types of things that would reduce inflammation because we are trying to do the opposite of what we have been taught in traditional arthritis. With traditional arthritis,

we use the anti-inflammatory drugs and things that block inflammation. With PRP and stem cells, we are trying to do just the opposite. We are trying to use inflammation as the subsequent healing cycle to actually create new tissue. A lot of the patients come from far distances, so we really have to outline to the physical therapist that they will be seeing at home that you cannot treat this patient like you would ordinarily treat a patient you have seen in the past. You must avoid ultrasound. You must avoid ice. You must avoid all the things that ordinarily you would use to reduce inflammation. You want to concentrate more on range of motion and strengthening. Those are the things that will eventually get the patient back to full activity.

Hauser: What do you foresee for the future of Prolotherapy and what would you like to see happen as it relates to the care of osteoarthritis in the United States?

Wei: I personally would like to see Prolotherapy used much more often. The reason is that a lot of the medications we use in traditional arthritis therapy carry with them a significant number of potential side effects. These side effects not only cause patients to have problems that are life threatening, but they also can cause problems that lead to death. I think we can use a type of treatment like Prolotherapy, that has been around for thousands of years, to try to regenerate lost tissue to speed up the healing process using a much more natural approach. Because that is what Prolotherapy and stem cell therapies are. I mean these are as natural as you can get. PRP is derived from the patient's own blood. Stem cells come from the patients themselves. To me, it makes much more sense to approach the conditions that we see using these new types of tools as opposed to using a lot of the dangerous chemicals that we have used in the past.

Hauser: Dr. Wei, thank you so much. I so much appreciate your time, and as a Prolotherapist, I would like to thank you for the work that you are doing.

Wei: Thank you. It has been a real honor to be in on this interview. ■

REMARKABLE RECOVERIES

My Journey Toward Wholeness: A Comprehensive Approach to Fibromyalgia Treatment from a Therapist-Patient Perspective

Jane E. Meyers, OTR/L

ABSTRACT

This article is a revealing personal case study of Jane Meyers, an occupational therapist who experienced symptoms of fibromyalgia during an extremely stressful period of her life. Through careful history, self-assessment and treatment from other medical professionals, she began a journey of healing from the pain and mental fog which accompanied her diagnosis. Though there appears to be no single cause of fibromyalgia, Jane learned that lack of REM sleep, stress, ligament laxity, fascial restrictions, deficient testosterone levels, candida and improper diet all played roles in her fibromyalgia complex. She followed a natural medicine protocol guided by Dr. Ross Hauser which included natural hormone replacement therapy, Prolotherapy to affected lax ligaments, anti-candida supplements, and several diet modifications. She found added relief with use of a magnetic mattress pad and pillow, treatment using John F. Barnes Myofascial Release (MFR), relaxation techniques and avoiding toxic relationships. She recovered from her pain and now uses her MFR training and life experience to help other patients in a clinic setting using myofascial release.

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KEYWORDS: fibromyalgia, fight or flight, John Barnes, ligament laxity, magnet mattress pad, myofascial release, NHRT, natural hormone replacement therapy, occupational therapy, Prolotherapy.

Through a long bout with fibromyalgia I have discovered both the fragility and resiliency of my body, mind and spirit. There were times I wondered during my recent trial by pain if I would ever see the light at the end of tunnel. It took diligent compliance and almost two years to regain my former status of vibrant good health.

My long and painful journey began eight years ago, late 2001. I had turned 42 a few months earlier but there seemed to be no ready explanation for why I was becoming so exhausted. What was going on? I exercised regularly and followed a careful diet, yet I was developing muscle pains. I began to hurt all over. I couldn't concentrate. Depression was setting in. Now exercise made the pain worse. I attempted simple yard work and was laid up for two days. Every physical effort created more fatiguing pain.

A full night's sleep still left me listless and drowsy all day. I couldn't stay awake after dinner. The aching got so bad I could no longer sleep in my bed. I resorted to an overstuffed couch to avoid pressure on my hips. The entire lower half of my body felt as if it were beaten and bruised. I got temporary relief from taking a hot bath every night and wrapping up in layers to keep in the heat.

Even more distressing, trying to get through a day of work became the biggest challenge. I used many sick days and went home early when I could. I wondered if it was narcolepsy, chronic fatigue, or MS. A mental fog accompanied every waking moment, hampering my memory, attitude, mood and motivation.

I considered seeking disability or medical leave because my work performance was significantly affected. But

Jane Meyers, OT, performing myofascial release on a client.

neither recourse was possible because I had become the sole provider for my new family: a young adult stepson battling cancer, two minor stepchildren and a husband. He turned out to be too mentally ill and emotionally stressed for regular work, while also trying to care for his very ill son.

My new home environment was not a nurturing, loving place. A single career woman until age 41, I had no life preparation for this avalanche. I didn't know where to turn for help. All I knew was that my body and mind were failing me. My quality of life had taken a sharp downward turn to a place I had never known. Independent and self-reliant for nearly 20 years, in my wildest nightmares I could not have imagined being so helpless. I had only my strong faith and a suffocating, but resilient, spirit.

A chiropractor assured me it wasn't MS. She mentioned fibromyalgia, but I denied that. Let me explain… We had started a home business selling magnetic wellness products. Several months before my symptoms, a nurse asked us to take part in a fibromyalgia fair. I offered to speak on using magnetic sleep products to promote stage 4 and REM/restorative sleep. I believed I knew what fibromyalgia (FM) was because I had researched one of the causes of FM: lack of stage 4 sleep. When I could, I slept on the magnet pad and I relied on the magnet pillow to stave off migraines. This was why I continued to disregard an FM diagnosis- I WAS sleeping. Too much!

I tried another avenue. I saw a massage therapist over spring break 2002. She was concerned about my legs. "I can pick up your (muscle) tissue right off your legs! It's stuck, like glued together, frozen. No wonder you're in so much pain! You really need to see Kelly." Kelly was an occupational therapist, like myself, who had a display at the fibromyalgia fair for her clinic, Wisconsin Center for Myofascial Release. I called her and we discussed my symptoms and the need for a doctor's order for therapy.

After I explained Myofascial Release (MFR) to my doctor she agreed I should try it. I initiated myofascial release treatments in May 2002. The prescription was twice weekly for six weeks using the John Barnes method of myofascial release. She wrote "Myofascial Pain Syndrome" as my diagnosis.

During most of the hour-long, hands-on treatments I remained passive, disconnected. From the massage table, I told of my intolerable home situation and the intractable stress. Kelly explained the fight/flight and "freeze" response to danger and stress, but in my state, I didn't connect the stress to my physical pain. I was in "survival mode." But I knew the home situation had to change. It was toxic and unsafe.

Later I read in John Barnes' book, *Healing Ancient Wounds*, that the "freeze" response is natural in all mammals who detect danger. "The preyed-upon animal will flee or attempt to fight, but if run to the ground it will enter a freeze response in which it assumes a state of immobility (think 'deer in headlights') while still manifesting high levels of activity of both the parasympathetic and sympathetic nervous systems. If the animal survives the attack, it will go through a dramatic period of discharge of this high-level autonomic arousal throughout the motor system. This discharge involves trembling, sweating, and deep breathing. This type of discharge is frequently seen in MFR patients after deep myofascial releases, followed by substantial improvement. As an example, in the case of a motor vehicle accident, a holding pattern or 'position in space' develops to protect the body against impact. As a result of the freeze response, this subconscious holding pattern is maintained indefinitely, manifesting sustained muscle contraction with resultant myofascial restriction,

WHAT IS MYOFASCIAL RELEASE?

Myofascial Release (MFR) is a hands-on technique that provides sustained pressure into myofascial restrictions to eliminate pain and restore motion. Fascia is a specialized system of the body that has an appearance similar to a spider's web or a sweater. Fascia (connective tissue) is very densely woven, covering and interpenetrating every muscle, bone, nerve, artery and vein as well as all of our internal organs including the heart, lungs, brain and spinal cord. The fascial system is one structure that exists from head to foot without interruption. Each part of the entire body is connected to every other part by the fascia, like the yarn in a sweater. In the normal healthy state, the fascia is relaxed and wavy in configuration and has the ability to stretch and move without restriction. Physical trauma, scarring, or inflammation, however, can cause the fascia to lose its pliability. It becomes tight, restricted and a source of tension to the rest of the body. Physical injuries, whiplash, surgery, habitual poor posture over time, repetitive stress injuries or shock and emotional distress have cumulative effects. The changes they cause in the fascial system influence comfort and the functioning of our body. The fascia can exert excessive pressure producing pain or restriction of motion, affecting flexibility and stability, and are a determining factor in our ability to withstand stress and strain. As treatment, the therapist uses a multitude of MFR techniques and movement therapy. Pain relief and improvement in function is also made through education in proper body mechanics and movement, the enhancement of strength, flexibility, and postural and movement awareness.

leading to chronic myofascial pain and tightness." The person may not be able to achieve a deep stage of sleep because the subconscious will be in a state of alert, ready to awaken at any moment to protect the self from danger.

Although I was aware of the fight/flight response from psychology courses, after reading John's book it became clear how my earlier symptoms may have started. From mid-2000 until late 2002, I was living with psychological danger. The person I married created an environment in which I felt defensive, on edge, and crazy with a self-protection I just shouldn't have, in what was supposed to be a honeymoon phase of marriage. Many days I felt bullied, though I stayed as long as I could for the sake of a sick stepson. One recourse our nervous system has is to retreat into ourselves, the "freeze" response to perceived dangers. And that freezing is what made my pain begin and be sustained. There was no "thawing" from the freeze. No trembling, sweating, or deep breathing out of it. My subconscious protective responses just continued daily and proved cumulative.

After six weeks of MFR treatment I enjoyed considerable pain relief because the therapist's hands allowed the facial restrictions or "frozen" tissue to release. My total Activities of Daily Living Pain Scale decreased from 30 to 4, an 87% change! My tolerance for performing activities like walking, sitting and standing increased from 15 minutes to one hour, and sleeping without pain went from five hours to six. Some left knee pain remained and became pronounced as the body pain was reduced, so my chiropractor ordered an MRI which showed a shredded meniscus and 14 cysts in the posterior patellar region. An orthopedic surgeon trimmed the shredded connective tissue. After a few weeks of PT, the knee pain subsided. I was advised prior to surgery, though, that my chances of getting osteoarthritis in that knee will be much greater due to the thinner meniscus. *Great…*

A bit of history now… Since getting four teeth extractions, orthodontia in my teens, and oral surgery at age 20 to extract five wisdom teeth, my bite became aligned posteriorly and I had developed TMJ pain, greater on the left. The extractions in my teens, if done today, would be considered poor practice. But it was standard practice in the mid-70's. The TMJ pain occasionally led me to resort to a liquid diet because chewing could cause facial muscle spasms. A few times the jaw locked open. At age 40, a tomogram showed a calcified, splintered ligament in my left cheek area, connected to the left TMJ. An oral surgeon advised TMJ surgery and two years of orthodontia to correct the damage and my bite. I couldn't begin to think of starting this complex course. As a therapist, I was able to step back and look at the bigger picture of my overall joint problems.

In childhood, I suffered many ankle sprains, had bilateral bunionectomies in my 20's, chronic bilateral trochanteric bursitis, and exhibited hypermobility in my finger joints and hips. I was always told to "stand up straight, stomach in, head back," but it was difficult to maintain. In time, I learned the connection between my joint flexibility, subluxations, TMJ pain, postural problems and an underlying hereditary ligament laxity problem. My forward head posture and jutting posterior were partly due to having **no** lordotic curve in my cervical spine. More surgery wasn't the answer, as I gladly discovered, Prolotherapy was.

I first heard of Prolotherapy at Caring Medical clinic. We had taken my stepson for a consult with Dr. Ross Hauser in the late summer of 2002. I read his Prolotherapy pamphlets and set them aside. During the many months of caring for my stepson and supporting the family under stressful conditions, I put my own needs last and some myofascial pain returned. In the summer of 2003, after a much-needed divorce, and my stepson's unexpected passing from a heart infection, I both grieved and rested. I felt I could focus on returning to my own sense of wholeness and I consulted with Dr. Hauser. I told him that an O.T., a chiropractor and a massage therapist all thought I may have FM. (FM is diagnosed by checking muscle trigger points. These often result from strain secondary to weak underlying ligaments around nearby joints.) After checking 18 trigger points and learning of my history of joint problems, Dr. Hauser agreed with the diagnosis. He ordered a number of tests including hormone panel, food allergies, blood pH and candida. I was treated with a "De-Yeast" supplement for candida and natural hormone replacement therapy (NHRT) for low testosterone, progesterone, estriol and DHEA. Proper testosterone levels in women are necessary to rebuild collagen, the connective tissue deficient in many FM patients.

Dr. Hauser advised me that it would likely take a full year to recover from FM *if* I followed this protocol. I was impressed with his demeanor and breadth of knowledge, and trusting my instincts I dedicated myself to getting well at whatever cost or inconvenience. This included

visiting Dr. Hauser's office monthly for Prolotherapy to affected joints, using hormone creams, avoiding allergenic foods which for me were egg whites and kidney beans, and following a prescribed diet. Prolotherapy treatment was concentrated to bilateral TMJ, cervical spine, knees, hips and lumbosacral regions. I took soft tissue support supplements and added more weight-bearing exercise to stimulate collagen growth. My diet excluded caffeine, artificial sweeteners and processed foods. Gluten tolerance is often in question with FM patients, so I decreased the amount of foods containing it. I avoided artificial stimulants, sleep aids and analgesics which would mask symptoms because I needed to feel myself getting better.

I often would count my "bad" days and "good" days. At first there were no good days, then gradually one or two days out of ten, and then more good days than bad after a year. I steered clear of toxic relationships and re-learned relaxation techniques. By the middle of 2005, I felt my FM symptoms had been resolved and the pain at Prolo treated areas was improved 85-100%. My energy level was up, mental fog had all but disappeared, sleep normalized and a positive attitude restored. The general quality of my life had gratefully blossomed, I was able to work without fatigue and I finally had time for a social life.

In the summer of 2006, I became interested in learning more about MFR. Because I was an O.T., I was qualified to take the courses, so I registered for the John Barnes MFR series. I wanted to help others recover from FM as I did. And, as fate would have it, Kelly asked me to join her practice. I have now added MFR as a part-time career and feel truly blessed that my life has come full circle. I am able to help others who are on their own journey toward wellness. When I meet a new patient, I share my story as an introduction to create a vision that they too can recover. I've discovered that most of my patients who have FM have suffered for five, 10, 20 years or more going undiagnosed and over-medicated. Although no single cause of FM has been determined and no standard "cookbook" approach to treatment, I believe if a patient is open to utilizing natural medicine, he/she can decrease recovery time. I can't help but feel that my relatively short period of suffering was God's grace to enable me to empathize, yet prepare me quickly for my work in helping them. With His guidance I charted my course, and pray others will allow themselves to be open to natural alternatives for healing.

Since my recovery, I have gone back for Prolo and MFR "tune-ups" once or twice a year to maintain function. I have also discovered Human Body Field analysis in the form of Nutri-Energetics Systems (N.E.S.) which uses infoceuticals to allow the body to heal itself using natural substances. N.E.S. has corrected my blood lipids, thyroid and spleen function, as well as reversed heavy metal concentrations. Following the Hausers' Diet Typing plan is an important aspect for health maintenance and is an emerging process for me. Eventually, I hope to be fully disciplined to that also. I now swim several times a week and am adding light weight training to my routine. While getting back into an exercise routine is a priority for me, I have to say I feel younger now than I did 12 years ago. My prayer is that my story will continue to help others become restored and feel vital again. ■

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REMARKABLE RECOVERIES

The Resolution of Grade I Lumbar Retrolisthesis with Prolotherapy: A Case Study

ABSTRACT

Prolotherapy is indispensable when considering biomechanical correction in the treatment of pain associated with ligament laxity. This 51 year old male was referred for assessment and treatment of a 15 year history of chronic low back pain. He had been very active his whole life and had sustained numerous injuries playing a variety of sports including hockey and football. He had been spending approximately $5,000 per year on massage therapy, craniosacral therapy, chiropractic care and standard physiotherapy. He was also put on a variety of medications including courses of anti-inflammatory medications, tricyclic antidepressants for analgesia, and benzodiazepines with no relief.

Physical examination identified laxity in his lower lumbar spine at levels L3, L4, and L5 as well as right sacrum. Concurrent examination by a manual orthopedic physical therapist (national examiner) demonstrated a flexion hypermobility at L5-S1, hypomobility at L4-5, hypermobility at L2-3, and right sacroiliac joint dysfunction.

X-ray from August of 2006 showed a grade 1 retrolisthesis of L4 to the L5 with suggestion of spondylolysis at L5 and facet arthropathy at L4-5 and L5-S1. Follow up images from July 2009, demonstrated no retrolisthesis, corresponding with relief of the patient's back pain.

After correction of the autonomic nervous system component of his pain with a German technique known as Neural Therapy (five sessions), and Prolotherapy (five sessions), with concomitant care by an experience physical therapist, his low back pain has been eliminated! He is active at both at work and play, and is off all medications.

This case emphasizes the importance of combined treatment modalities, Prolotherapy being paramount, to elimination of even long standing pain.

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KEYWORDS: low back pain, lumbar spine, neural therapy, physiotherapy, Prolotherapy, retrolisthesis.

The Physician's Perspective

Robert Banner, MD

People want to be healed! For many with chronic pain, they are told there is nothing else that can be done. They are told to live with the pain and cope as best they can. This is simply not true!

In October of 2006, I saw Freddie Smith with a complaint of at least 15 years of chronic low back pain that interfered with all aspects of his life. He was told by a friend that Prolotherapy might be helpful for him. He had been to a number of therapists, trying multiple modalities and different types of medications used in "pain management." He was spending at least $5,000 per year out of pocket for these modalities. Quite a sum of money in a country with universal health care where people are not used to paying for any of their health care related expenses. He was skeptical of any other treatments and was anxious about any injection therapies, especially when he had to pay for them.

He presented with X-rays from 2006 that showed a grade I retrolisthesis or movement of one vertebra on another at the fourth and fifth lumbar level with associated X-ray damage seen of the facet joints at this level. (*See Figure 1.*) This is consistent with laxity of the ligaments at this level. Physical examination found tenderness to palpation at the levels of the third, fourth and fifth lumbar vertebrae as well as the right sacroiliac joint. In Canada, a physiotherapist who takes additional training and examinations in orthopedic manual medicine (manual orthopedic physical therapists) is considered an expert in assisting in the diagnosis and recovery of patients such as Freddie. He was also seen by one of six national examiners for manual orthopedic physical therapy who found areas of hypo (decreased) and hyper (increased) mobility in his lumbar spine as well as various factors related to de-conditioning brought on by his longstanding pain.

Prior to beginning any injection therapies, I believed he would benefit from such care that would only enhance his response to Prolotherapy. While this treatment was ongoing, I began a course of five neural therapy treatments The area of treatment for neural therapy involved injection of 0.5% procaine without preservative and buffered to a pH of 8.0 to areas identified as interference fields. These are areas of autonomic dysfunction. In this case, I used a form of applied kinesiology known as Autonomic Response Testing to localize the problematic areas and treat. They were areas of previous surgical scars that had a role to play in the patient's appreciation of pain. If you will, the autonomic component or "nerve" component of the mechanical pain with its foundation in instability. This German technique for balancing the autonomic nervous system is, at times, important to deal with the nervous system component of pain sensation. Once the neural therapy was completed, the addition of appropriate physical therapies primed the patient for success with Prolotherapy. The Prolotherapy solution used was 25% glucose with 1% lidocaine and 0.25% Marcaine® at levels L4, L5 and S1. This was done at monthly intervals, three times, and then again on two occasions five months later. At this point, Freddie no longer had back pain, was able to work and participate in sports and was off all medications! His follow up X-ray report showed no associated retrolisthesis consistent with his absence of back pain! (*See Figure 2.*) The two X-ray reports were interpreted by two different radiologists.

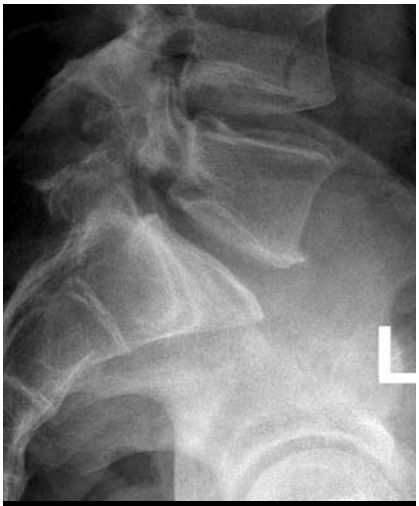

Figure 1. 2006 X-ray showed grade I retrolisthesis of L4-L5.

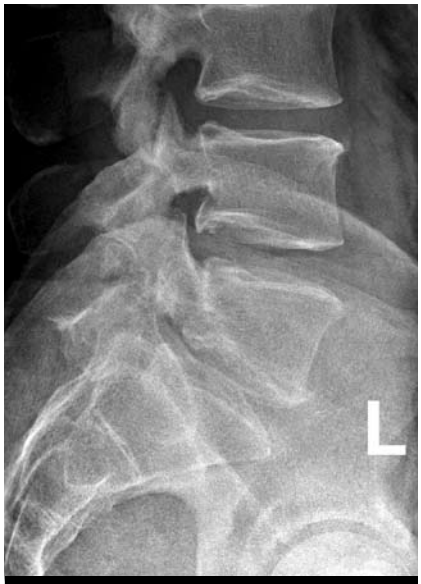

Figure 2. 2009 X-ray not reporting retrolisthesis of L4-L5, as was previously reported before receiving Prolotherapy/physical therapy combination. At the time of this X-ray, the patient reported no pain and was able to discontinue his pain medication.

The Orthopedic Physical Therapist' Perspective

Rob Werstine, PT, FCAMT

Mr. Smith was referred to physiotherapy (manipulative physiotherapist) for low back pain from Dr. Banner, and at that time, had not yet had Prolotherapy. Using the patient specific outcome measure, where Mr. Smith identified sleeping, hockey, golf and driving as important activities, he rated his ability to perform each of these four activities on a separate 5-point scale where four is "satisfactory" and zero indicated "completely unable." His total score after rating each activity was 1 out of 16, indicating very poor function.

On initial assessment, in addition to the hyper and hypomobile segments that were identified, the most striking feature was postural. His lumbar spine was always flexed. (*See Figure 3.*) A length-tension and strength assessment of his lower quadrant found stereotypical weaknesses that are associated with a flexion pattern of the lumbar spine: short hamstrings, weak hip abductors, gluteal weakness, delayed gluteal firing with leg extension, and a positive active straight leg raise, which indicates poor core stabilization strategies in the lumbar and sacroiliac areas.

The initial six weeks of treatment focused on three main issues: lack of pelvic dissociation, poor hamstring length bilaterally and poor core stability. Improving pelvic dissociation and improving hamstring flexibility were treated with complimentary exercises. Using a hyper-lordotic position in sitting, Mr. Smith attempted to straighten his legs one at time, holding each time for five seconds. Pelvic dissociation was also practiced in standing, with arms straight and hands resting flat on a high bed. He was instructed to repeat each exercise ten times at least four to five times per a day, with the expectation being to improve the endurance of the postural muscles.

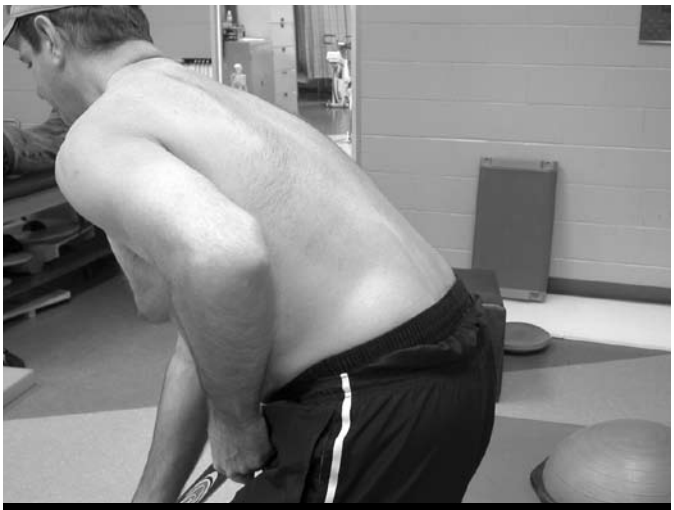

Figure 3. On initial assessment, patient in his functional stance for hockey. Note the reversal of the lumbar lordosis.

Figure 4. Positioning for a right-sided L4-5 gapping manipulation.

Improvement of the global core stabilizers like the gluteal muscles and hip abductor muscles are necessary to improve functional core stability through dissociation of hip movements from pelvic movements. Initially, Mr. Smith was only able to lift his knee 10 centimeters with hip abduction/external rotation in a side-lying position, but he progressed to lifting through full range over an eight to nine week period. To improve hip extension strength, he performed a simple bridging exercise, which also improved drastically. Specific core stabilization exercises as outlined by Richardson in Therapeutic Exercise for Spinal Segmental Stabilization in Low Back Pain, 1999, was concurrently initiated. Manual traction to decrease leg pain was initiated at this time, and a manipulation of the right ilium into anterior rotation was performed on seven occasions when the leg length discrepancy was observed.

From six to twelve weeks, exercises were made more difficult by adding multiple planes of movement and functional patterns of movement. During this phase, a specific gapping manipulation of L4-5 on the right was used, which decreased the right leg pain and right side back pain. (*See Figure 4.*) A combination of Prolotherapy treatment, manual therapy and core strengthening exercises abolished Mr. Smith's pain with sleeping and activities of daily living (ADL's). In January of 2008, Mr. Smith scored a 14 out of 16 on his patient specific outcome measure stating that he was no longer awakening at night because of his back. In addition, golf and driving were not limited at all by his back pain. But, most importantly, he had taken control of his posture—a very successful outcome! (*See Figure 5.*)

Figure 5. At discharge, patient in his functional stance for hockey. Note the maintenance of the lumbar lordosis.

The Patient's Perspective

Freddie Smith

I was sitting on the weight bench the other day and it suddenly hit me... I did not feel any pain, tingling in my extremities, shooting pain down my legs, numbness, or pain in my feet. I realized just how far I had come in the last three years. The fact of the matter is I do not know, but I want to relive the journey, if to help someone else who is suffering from similar ailments, or if only for myself, but to understand how I got to this point.

I remember, as far back as a young boy, suffering lower back and SI pain. Even in grade school it hurt to sit down, to skate, or run. Back then we were told not to complain, and really there was no one to complain to. Over the years, I played many contact sports: hockey, football, baseball, basketball. You name it, I loved to play it. But all with a degree of pain and lack of mobility in my lower back and SI, which I just got used to. It frustrated me, as I knew it stopped me from being the best I could be and from playing at a level I was capable of, or even moving on to higher levels. I am sure the weight lifting, heavy lifting summer jobs, etc… all played their part, as did, perhaps, genetics. I would have been in my teens when I first saw a surgeon. It left me in a very grey area, I was in pain, but could live with it, and there was no cure.

As time went on, I continued to play hockey and baseball, but the pain got worse and made harder to function on the field and on the ice. I also worked out, but even that was painful. It got to where anything I enjoyed doing, from golf to going for a walk, was a very painful experience. I maintained the ability to function, albeit in pain, from my chiropractor. But even his help, after years of keeping me active, could not keep me playing the sports I love and performing day to day tasks, such as cutting the grass, walking, and even sleeping. I had pain going down both legs and feet. I could not drive my vehicle without extreme pain in my legs, feet, and SI. I could not bend over to put my socks and shoes on. Cutting the grass and gardening were very painful. I was only in my 40's with still no help in sight.

I was fortunate to meet a lady who referred me to Dr. Banner's practice. After our initial consultation, the pain and frustration was so bad I just wanted him to treat me no matter what. Luckily for me, I was in good hands. Dr. Banner first referred me to Rob Werstine at The Fowler Kennedy clinic, which is a first-rate facility, and Rob is certainly a first-rate therapist. It was then, in talking and working with him, I first realized how bad things were and how far I had to go. He had me doing beginner's exercises which I could not do without help. I remember the long hours spent just to try and squat properly with my bad back.

It was time for Prolotherapy, and Dr. Banner injected me on my bad side first. I followed that up with lots of hard work in physiotherapy. Then he injected the other side, and again back to the bad side. Then a last set of injections into the other side again.

Freddie (on the left) with his golf buddy.

It has been over two years since my first injection. I work out for an hour and a half daily, golf, play pick up hockey, and sleep at night, all without pain shooting down my legs. I can bend over, drive the car (longest drive was 16 hours in a 20 hour period so far), and do the daily things we take for granted without pain.

The guidance of Dr. Banner and his Prolotherapy, in conjunction with Rob Werstine and his physiotherapy, has given me a second chance to enjoy the things that made my life fun. Rob tells me my back is strong enough now that I could kick the hockey up a notch, but one thing at a time. I have a handicap that needs to come way down on the golf course, as I only played a couple of times a year, due to the pain. I look back at all the pain, hard work, and therapy, and I realize the one thing that made it all worthwhile was being able to play shinny hockey with my six year-old nephew and his friends, on his backyard rink this winter. I play with no pain, after not skating for two years.

I want this to be a letter of hope for people who suffer like I did. There is hope out there now. There are great programs and treatments such as Prolotherapy, and the teamwork with therapists like Rob, offer so much hope to so many. I never stopped working out, even in pain, and was able to workout through my treatments. I am in far better overall shape now and pain-free. I hope someone who suffered or is suffering needlessly, like I did for so long, reads this and realizes there is hope. ■

WONDER WHY?

The Theoretical Basis for and Treatment of Complex Regional Pain Syndrome with Prolotherapy

Ross A. Hauser, MD & Debra K. Brinker, RN

ABSTRACT

Complex regional pain syndrome (CRPS) typically refers to post-traumatic pain that spreads from the site of injury, exceeds in magnitude and duration the expected clinical course of the inciting event, and progresses variably over time. Burning pain is the primary symptom, but patients frequently report allodynia, changes in the color or temperature of the skin, and if the condition progresses, trophic changes of the skin, nails, and bone occur. The condition produces a high degree of suffering, lost productivity and cost of treatment. While there are many theories as to why CRPS occurs, success in treatment of CRPS with traditional medical therapies is dismal.

CRPS generally appears following a physical trauma, involving the bone and soft tissues which are treated with long periods of immobility. While this immobility itself may be needed to heal a bone injury such as a fracture, it encourages ligament injuries to not heal. Stress deprivation or immobility causes a protracted state of progressive atrophy and lack of mechanical strength in the injured ligaments. The high density of both myelinated and unmyelinated nociceptors in the non-healed ligaments then become sensitized to the point that even normal or less than normal activities activate them to fire causing severe burning pain. These activated nociceptors through local and feedback loops in the central nervous system, cause autonomic phenomenon in the extremity including referral pain, edema and temperature disturbances. Research by George S. Hackett, M.D., who coined the term Prolotherapy, found that ligament relaxation (his term for non-healed ligament injuries) caused bone dystrophy (osteopenia/osteoporosis), which is a common feature of CRPS. He also noted that ligament relaxation often activated the sympathetic nervous system and that when Prolotherapy was performed to the injured ligament(s), not only did the local pain remit, but so did the autonomic phenomenon. Since traditional treatments do not address non-healed ligament injuries, this entity could be the reason that so many cases of CRPS are never resolved. Since Prolotherapy causes ligament regeneration, it should be in the arsenal of any clinician treating patients with unresolved CRPS symptoms.

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KEYWORDS: allodynia, CRPS, chronic regional pain syndrome, ligament injury, nociceptors, Prolotherapy, RSD, reflex sympathetic dystrophy, sympathetic nervous system.

INTRODUCTION

Complex regional pain syndrome (CRPS) is a chronic pain and potentially disabling syndrome which typically affects the extremities. It is characterized by a variety of autonomic and vasomotor disturbances, of which diffuse pain, spreading edema, temperature disturbances, and functional impairment are most prominent.[1] CRPS generally appears following a physical injury, is disproportionate to the precipitating event or level of tissue damage, progresses inconsistently over time, and is associated with nonspecific signs and symptoms.[2] It is a disease with an unpredictable and uncontrollable nature, and is a syndrome covered in controversy and confusion.[3, 4] CRPS may appear at any age, indiscriminately affecting young and old, male and female. It spreads like wild fire, perhaps starting in the foot, moving its way up to the knee and back, then down the other leg, and up into the arms.

SIGNS AND SYMPTOMS OF CRPS

Complex regional pain syndrome typically refers to post-traumatic pain that spreads from the site of injury, exceeds in magnitude and duration the expected clinical course of the inciting event, and progresses variably over time. It is characterized by a variety of nonspecific symptoms and signs. (*See Figure 1.*) In a large sample of patients, 81% noted burning or stinging pain as the number one symptom.[5] Patients frequently report allodynia, where the skin becomes so exquisitively sensitive to touch or temperature that normal light contact, such as clothing touching the skin or a draft blowing on the affected area, produces severe pain.[6] Other common symptoms of CRPS include changes in the color or temperature of the skin, asymmetric sweating, trophic changes of the skin, nails and hair.[7] Galer et al. noted that the most common symptoms included severe pain (100%), abnormal swelling (96.7%), and weakness (96.7%). Other initial symptoms were abnormal coldness or heat, color changes, inability to move an extremity, muscle spasms, abnormal sweating, tremors, skin dryness, and feelings as though the

Signs and Symptoms of CRPS

- Abnormal swelling/edema
- Allodynia
- Change in skin color
- Change in skin temperature
- Changes in skin, hair, and nail growth
- Decreased ability to exercise
- Feeling of limb disconnect
- Hyperalgesia
- Hyperesthesia
- Hyperpathy
- Inability to move extremity
- Incoordination
- Involuntary movements
- Limited range of motion/movement
- Muscle and skin atrophy
- Muscle spasms
- Osteoporosis
- Paraesthesias
- Paresis
- Pseudoparalysis
- Severe pain
- Sweating asymmetry
- Tremor

Figure 1. The signs and symptoms of complex regional pain syndrome (CRPS).

limb were disconnected.[8, 9] The swelling may spread with accompanied muscle and joint stiffness. CRPS patients may then experience limited movement in the affected area, with atrophied muscles, limited range of motion, and possible contractures.[10]

HISTORY AND NOMENCLATURE

CRPS has gone through a progression of names. The first description of CRPS may have dated back to 1634 when King Charles IX suffered persistent pain following a bloodletting procedure.[11] In 1872 an American Civil War physician, Weir Mitchell described cases of a burning pain syndrome following gunshot wounds as causalgia.[12]

"*We have some doubt as to whether this form of pain ever originates at the moment of wounding…Of the special cause, which provokes it, we know nothing, except that it has sometimes followed the transfer of pathological changes from a wounded nerve to unwounded nerves, and has then been felt in their distribution, so that we do not need a direct wound to bring it about. The seat of the burning pain is very various; but it never attacks the trunk, rarely the arm or thigh, and not often the forearm or leg. Its favorite site is the foot or hand…Its intensity varies from the most trivial burning to a state of torture, which can hardly be credited, but reacts on the whole economy, until the general health is seriously affected…The part itself is not alone subject to an intense burning sensation, but becomes exquisitely hyperanesthetic, so that a touch or tap of the finger increases the pain.*" –Silas Weir Michell, 1872

In 1900, Paul Sudeck described an extremity pain syndrome which developed after bone fractures, which was referred to as Sudeck's syndrome and in European countries as Sudeck's Atrophy.[13] Other names have included minor causalgia, post-traumatic pain syndrome, post-traumatic painful arthrosis, Sudeck's dystrophy, post-traumatic edema, shoulder-hand syndrome, chronic traumatic edema, algodystrophy, peripheral trophoneurosis and sympathalgia.[14] Based on the experience that some patients were obtaining relief from sympathetic blocks, the term Reflex Sympathetic Dystrophy (RSD) was introduced in 1946 by J.A. Evans to accommodate the role of the sympathetic nervous system.[15] The term Sympathetically Maintained Pain was introduced in 1986 as a synonym of RSD.[16] Then due to lack of pain relief in some patients after sympathetic block, the term sympathetically independent pain was used to describe pain states similar to RSD.[17] In an effort to clarify the nomenclature, the International Association for the Study of Pain met in 1993 and came up with the term Complex Regional Pain Syndrome.[18] (*See Figure 2.*)

Names for CRPS

- Algodystrophy
- Causalgia
- Chronic traumatic edema
- Complex regional pain syndrome
- Minor causalgia
- Peripheral trophoneurosis
- Post-traumatic edema
- Post-traumatic pain syndrome
- Post-traumatic painful arthrosis
- Reflex sympathetic dystrophy
- Shoulder-hand syndrome
- Sudeck's atrophy
- Sudeck's dystrophy
- Sudeck's syndrome
- Sympathalgia
- Sympathetically independent pain
- Sympathetically maintained pain

Figure 2. Nomenclature has changed through history regarding this disease. In 1993, the International Association of the Study of Pain (IASP) coined the term complex regional pain syndrome (CRPS) to embody all of the above names.

DIAGNOSIS AND DIAGNOSTIC CRITERIA

The nature of, diagnostic criteria for, and even the naming of CRPS have been controversial.[19] *See Figure 3* for the IASP Diagnostic Criteria.[20] Taking into consideration the controversy in nomenclature, the Special Interest Group "Pain and the Sympathetic Nervous System" of the International Association for the Study of Pain (IASP) at a workshop in Orlando in 1993 came up with the new name after "extensive grappling."[21] Robert A. Boas describes the terminology, "The umbrella term for all disorders falling within the domain of causalgia and reflex sympathetic dystrophy was now designated as a complex regional pain syndrome (CRPS). *Complex* describes the

Diagnostic Criteria for CRPS

1. The presence of an initiating noxious event, or a cause of immobilization.
2. Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event.
3. Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain.
4. This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

Figure 3. International Association for the Study of Pain (IASP) criteria for someone to meet the diagnosis of complex regional pain syndrome (CRPS).

varied and dynamic nature of the clinical presentation within a single person over time, and among persons with seemingly similar disorders. It also included the features of inflammation, autonomic, cutaneous, motor, and dystrophic changes, which distinguish this from other forms of neuropathic pain. *Regional* – as in the wider distribution of symptoms and findings beyond the area of the original lesion—is a hallmark of these disorders. Such symptoms and signs usually affect the distal part of a limb but occasionally can involve discrete regions or spread to other body areas. *Pain* is the *sine qua non* for the CRPS syndrome—pain that is disproportionate to the inciting event. This is not just burning pain, but includes spontaneous pain and thermal or mechanically induced allodynia. *Syndrome* – the constellation of symptoms and signs of CRPS represents a series of correlated events that are sufficient to be designated as a distinctive entity, even though we are not sure what constitutes each of these events, or which are essential, nor the nature of the pathological changes that ensue."[22]

There are three classifications of this syndrome. CRPS type I usually occurs after an illness or injury that did not directly damage the nerves in an affected limb or region of the body. It was previously termed reflex sympathetic dystrophy (RSD), but the current research suggests multiple causes rather than the sympathetic nervous system as the culprit. Complex regional pain syndrome type II, formerly known as causalgia, has been commonly distinguished by evidence of neuronal damage. However, recent studies suggest that there may not be a clear distinction between the syndromes.[23] CRPS III was created for the difficult cases that contained pain and sensory changes, with either motor or tissue changes, but did not comply fully with the more classical forms.[24, 25]

The diagnostic criteria are not yet optimized or even standardized in the literature, and there is reportedly no noticeable difference since the introduction of the criteria.[26-28] Although the criteria are an important step in the right direction, they lack specificity, which makes it difficult to determine new treatment approaches targeted at particular pain mechanisms.[29, 30] There are several other clinical criteria, including Bruehl's or Veldman's clinical criteria, however the IASP criteria are cited more widely in the literature and treatment trials.[31] Stages of progression of CRPS have also been set forth, however an eight year study of 829 subjects failed to identify these stages.[32] A second IASP conference in 2000 also rejected the concept of staging.[33]

HOW COMMON IS CRPS?

There are only a few published epidemiological studies regarding the incidence of CRPS in the general population. The most recent studies by M. de Mos began in 1992 with ongoing data collection utilizing electronic patient records.[34] The first of two de Mos studies included 600,000 patients throughout the Netherlands from1996-2005.[35] The conclusion of the study was an incidence rate of CRPS at 26.2 new cases per 100,000 annually.[36] Applying the results from the de Mos study to the U.S. census bureau population estimates of 299,665,000; one would expect over 50,000 new cases of CRPS-I annually.[37] Most of these patients are at an economically productive age, but CRPS seriously limits their ability to work. The Reflex Sympathetic Dystrophy Foundation conducted a study of 1,348 CRPS patients and found that work was seen to increase pain in 79% of the cases, 38% were unemployed, 17.4% worked full time, 8% part time, and 21% worked at one time but had to stop because of CRPS.[38]

In another study from 2006 of 168 patients, 28% were officially disabled because of CRPS, and the cost of physical therapy for a year per patient was estimated at $6,000.[39] The costs for physical therapy alone for the officially disabled percentage (28-38%) of 50,000 new cases annually calculates to 84-114 million dollars per year. This does not take into account the cost of therapy for those who are not considered officially disabled, or the surgery, or the pain medications, etc. It is clear that CRPS is a disabling disease and has a severe impact physically, vocationally, and economically. Michael Rowbotham, MD comments, "Overall, the present situation is most

unfortunate, considering the very high burden of suffering, lost productivity, and a cost of treatment that may exceed $100,000 (per patient)."[40]

THE CAUSE OF CRPS

Clearly, a substantial number of patients are at risk for and will develop CRPS each year. What then is the precipitating factor of this disabling syndrome? CRPS may develop after a traumatic injury or without any obvious trigger event. A chart review by Birklein et al. of 145 patients in 2000, suggested 41.3% of cases were due to fractures, 32% from soft tissue injuries, 9% due to surgeries, and 17.7% from minor traumas and lesions.[41-43] In the Duman study from 2006, which included 168 patients from two hospitals, the percentage of CRPS from fractures was 55.3%, from soft tissue trauma was 28%, and 16.7% from incisive injuries.[44] A review of 140 cases at the Mayo Clinic over a two year period also noted 65% from external trauma including 28.6% after soft tissue trauma, 20% after fractures, and 16.4% of those cases were a result of surgery.[45] In the majority of pediatric cases, CRPS follows a soft tissue or joint injury.[46] It is perceivable that the aforementioned 55-65% of trauma cases including sprains, fractures and surgery also involved damage to the soft tissues including ligaments. If we were to imagine the force required to break a bone, we could also appreciate that the ligaments supporting the joints would also be injured. Connelly et al. comments, "It should be emphasized that the energy of injury is transferred to the soft tissue as well as to the bone. It is easy to forget this when we mistakenly emphasize the radiograph in our acute evaluation of injuries. Soft tissue injury occurs directly when an object impacts it and occurs indirectly when it is stretched, twisted, or torn at the instant of injury. The soft tissue envelope is the key to understanding most problems in fracture care."[47] The injured soft tissue includes the ligaments and tendons. Ligaments are bands of flexible, tough, dense white fibrous connective tissue which attach one bone to another bone. Tendons are bands of dense fibrous tissue forming the termination of a muscle and attaching the muscle to the bone.[48] Ligaments stabilize and support the joints through their full range of motion, therefore an injury to the ligament negatively affects the joint mechanics.[49] *Is it possible that this ligament injury is involved in the subsequent development of some forms of CRPS?*

It has been noted that the majority of CRPS cases occur after orthopedic procedures.[50] To further delineate the frequency of CRPS as far as fractures, a study of 109 patients indicated an incidence of CRPS at 25-37% after wrist fractures.[51, 52] In the group of 145 patients with CRPS, 42% had previous fractures.[53, 54] In the second de Mos study of 186 CRPS patients, a fracture was the most common precipitating injury in 49% of the cases.[55] As far as surgery, the estimates include 2.3-4% after arthroscopic knee surgery, 2.1-5% after carpal tunnel surgery, 13.6% after ankle surgery, 0.8-13% after total knee arthroplasty, and 7-37% after wrist fractures.[56] Reuben noted that the development of CRPS is a common complication after fasciectomy for Dupuytreen contracture giving an estimate of 4.5-40%.[57, 58] (*See Figure 4.*)

Figure 4. CRPS precipitating events. Fracture and soft tissue injury are the most common precipitating events leading to CRPS.

Study name	Duman [44]	Mayo Clinic [45]	Birklein [41-43]	de Mos 2006 [35]	de Mos 2008 [55]
Patient #'s in study	**168**	**140**	**145**	**238**	**186**
Fracture	55.3%	20.0%	41.3%	43.5%	49.0%
Soft tissue injury	28.0%	28.6%	32.0%	22.6%	26.0%
Surgery	16.7%	16.4%	9.0%	13.6%	11.0%
Spontaneous		15.0%		10.6%	8.0%
Other events, lesions, minor trauma, injections		19.0%	17.7%	9.6%	6.0%

As stated earlier, these fractures and surgeries cause soft tissue damage involving the ligaments. (The reverse is also true; weakness of the ligaments could have caused the bony structure to be susceptible to fracture.) Blood supply to bone is excellent, whereas blood supply to ligament tissue is poor. If the blood vessels supplying blood to the ligaments are sheered by fracture or surgery, this further impedes the ability of the ligaments to heal. (*See Figure 5.*) The ligaments (and other soft tissues) not healed, sets up a perpetual cascade leading to CRPS. We will continue to explore the role of ligament injury and the development of CRPS later in this article.

ALTERED PHYSICAL FUNCTION, QUALITY OF LIFE, AND DISABILITY

Patients with CRPS will face significant quality of life consequences as this pain syndrome dramatically alters their lives as well as the lives of their families and

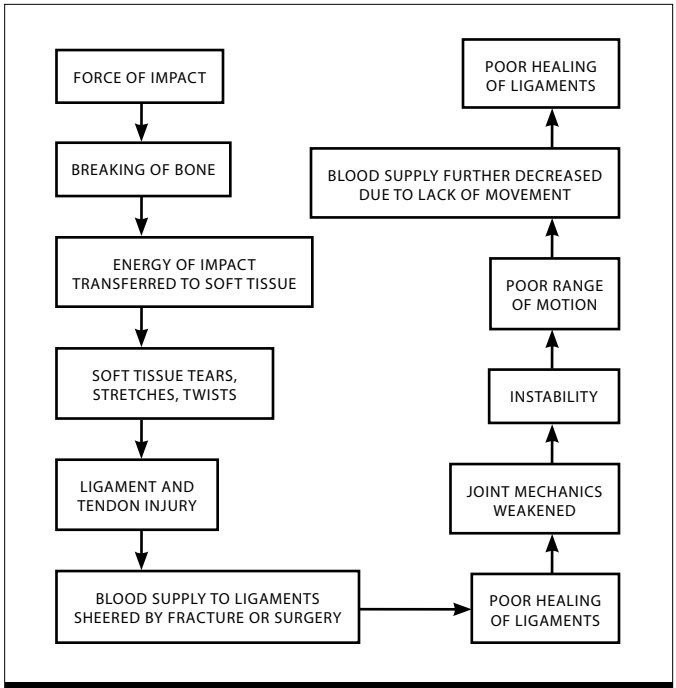


Figure 5. How trauma leads to poor healing of ligaments.

friends. As noted previously, the effects of CRPS can potentially lead to permanent disability. Galer et al. noted that a majority of patients felt that symptoms caused "substantial interference" with general activities (74%), mood (74.2%), mobility (67.7%), normal work (74.2%), relations (64.5%), sleep (67.7%), and social activities (74.2%). Interference in self-care was identified in 45.2%. This study also noted the mean duration of CRPS in the 31 patients surveyed to be 3.3 years. The need to use a device, such as a cane, walker, or wheelchair, was reported by 35% of the participants. The participants in the Galer study reported moderate to severe pain intensity with substantial disability.[59] A survey of CRPS patients by the RSD Foundation found that 23% of the respondents had to stop daily activities occasionally due to pain, 74% had to stop them frequently due to pain, and 87% suffered from constant or nearly constant pain.[60] These reports confirm that CRPS can have a very constricting effect on functional capacity. Caregivers of 51 CRPS patients were reported to suffer significant strain, low mood and poor adjustment.[61] A study of 65 patients noted 30% of RSD patients had to stop work for more than a year. (*See Figure 6.*) They also noted high rates of unemployment and financial compensation, establishing RSD as a disabling disease.[62, 63] In the retrospective chart review of 134 patients, 54% had a workers' compensation claim related to the CRPS, and another 17% had a lawsuit. This is consistent with another study noting that 64% of those surveyed had a work related injury resulting in their symptoms.[64, 65] CRPS is a syndrome that causes millions of Americans to suffer from chronic, unremitting pain.

WHAT ARE THE MECHANISMS BEHIND CRPS?

The mechanisms triggering the pain as well as the associated changes that occur in patients with CRPS remain largely obscure. As with other factors surrounding CRPS, the pathophysiology is also unclear. Divergent theories abound since the spectrum of presentations of this syndrome is so diverse.[67] Multiple components have generally been proposed as the pathophysiological mechanisms, and hypothesis include a neuropathic mechanism which is sympathetically maintained, an immunological mechanism including inflammation, and an altered expression of human leukocyte antigens. The hypotheses exist for both peripheral and central mechanisms. None of this data however is conclusive.[68] They may include the somatic and visceral sensory systems, the central control systems, the sympathetic nervous systems, the somatomotor system, and the neuroendocrine systems.[69] These systems are further differentiated to include the following symptoms noted in CRPS: (1) The nociceptive system: spontaneous pain, hyperalgesia, allodynia. (2) The sympathetic nervous system: abnormal regulation of blood flow and sweating. (3) Sympathetic nervous system, afferent system: edema of the skin and subcutaneous tissues. (4) Sympathetic system,

Figure 6. The percentage of participants in the Galer Study who felt that CRPS affected these activities of daily living, and the percentage of participants in the RSD Foundation Study who changed their daily lives due to the pain from CRPS.

Galer Study	
General activities	74.0%
Mood	74.2%
Mobility	67.7%
Normal work	74.2%
Relations	64.5%
Sleep	67.7%
Social activities	74.2%
Self-care	45.2%
RSD Foundation Study	
Frequently stop activities	74.0%
Occasionally stop activities	23.0%
Constant/nearly constant pain	87.0%

afferent system, somatomotor system: trophic changes of skin, appendages of skin, and subcutaneous tissues. (5) Somatomotor system: active and passive movement disorders, including physiological tremor.[70] A more recent mechanism set forth in explaining the pathophysiology of CRPS is an inflammatory response. An unknown stimulus induces an excessive production of inflammatory mediators, leading to an imbalance in production and clearance of toxic radicals. This excessive production of oxygen radicals results in destruction of healthy tissue.[71] (*See Figure 7.*)

Possible CRPS Mechanisms

- Afferent system involvement
- Altered expression of leukocyte antigens
- Central control mechanisms
- Central mechanisms
- Deactivation pain theory
- Genetic predisposition
- Immunonologic mechanism
- Inflammatory mechanism
- Neglect theory
- Neuroendocrine system involvement
- Nociceptive system involvement
- Peripheral mechanisms
- Somatic and visceral mechanisms
- Somatomotor system involvement
- Sympathetic nervous system involvement
- Sympathetically maintained neuropathic mechanism

Figure 7. Proposed mechanisms and theories behind CRPS.

Animal studies involving ligation of the L5 spinal nerve in rats demonstrate that these animals develop similar symptoms (allodynia) as CRPS patients. Subsequent surgical sympathectomy reportedly showed significant reversal of these symptoms, demonstrating a sympathetic component.[72] There are studies, however, involving L5 nerve ligation of rats noting that neuropathic pain behavior does not depend on the sympathetic nervous system.[73] Other studies show neuropathic pain behavior possibly resulting from a mechanical injury to a peripheral nerve.[74] CRPS may also be triggered by the arrival in the central nervous system of a transmission like injury discharge, produced by traumatized tissues (ligaments/tendons) with or without nerve injury.[75] CRPS may involve damage to small diameter nociceptive fibers.[76] A nociceptor is a sensory receptor that sends signals that cause the perception of pain in response to a potentially damaging stimulus. Nociceptors are silent receptors and do not sense normal stimuli. Only when activated by a threatening stimulus do they invoke a reflex, as would occur when a ligament or soft tissue is injured.[77] (*See Figure 8.*)

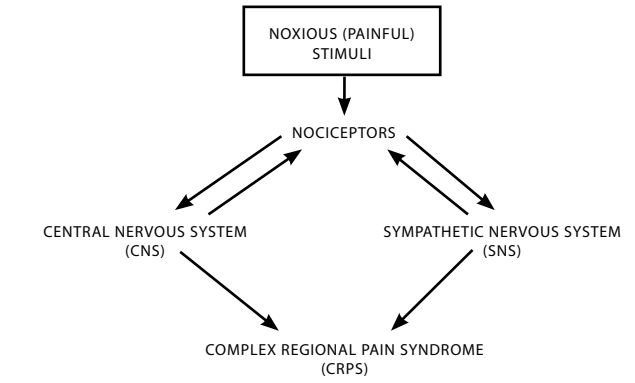


Figure 8. Nociceptors and CRPS. Any noxious or painful stimuli can activate nociceptors which sets up a cascade involving the central nervous system (CNS) and sympathetic nervous system (SNS) resulting in CRPS.

It is also proposed that there is a genetic predisposition to CRPS.[78] The conclusion set forth after years of patient observation and research on humans and animals, is that CRPS is a complex neurological disease, involving the brain at several integrative levels.[79]

TESTING FOR CRPS

There are no specific diagnostic tests for CRPS which can reliably confirm or exclude the diagnosis.[80, 81] Diagnostic criteria is purely clinical.[82-84] It is based on history and physical examination and is not determined by test results, since the utility of diagnostic tests has not been demonstrated.[85-87] Although there is no definitive test for CRPS, physicians try to use such tools as volumetry to measure edema, thermometry to measure skin temperature differences, and resting sweat output (RSO) to measure sweating, however it is not clear that objective measurement is precise. This instrumentation is used to measure clinically apparent signs like those included in the diagnostic criteria, however due to the confounding nature of CRPS, ie. changing body temperature, time of day, and exact placement of the device, it is unclear if objective measurement is even practical.[88] Testing may be invasive or noninvasive, but data is not available for sensitivity or specificity of the tests.[89] In a study comparing testing to clinical diagnosis, instrumentation added little to the overall accuracy of diagnosing CRPS type I, while no single test identifies all persons with CRPS.[90, 91]

A myriad of diagnostic tests have been studied for CRPS. Bone scans may be normal or show increased or decreased uptake in CRPS.[92] (*See Figure 9.*) The bone scan also suffers from the subjective interpretation of the radiologist. Furthermore, researchers disagree on its adequacy, specificity, and sensitivity.[93, 94] Tourniquet ischemia test appears to produce a progressive blockade of nerve transmission, but the interpretation of this test is under intense scrutiny. Plain radiographs help rule out issues such as fractures, which may be responsible for the symptoms, but for CRPS there are no radiographic changes or evidence of osteoporosis in the acute phase.[95] Radiographic demineralization may be noted in the later phase of CRPS using X-rays when comparing the affected area with a normal area, however this is also noted with disuse or immobilization of the limb. Other tests like EMG's, laser Doppler, and microneuronographic measurement of peripheral sympathetic function also have not yet proven their utility.[96] MRI may show nonspecific soft tissue changes.[97] Sympathetic nerve blocks were once considered diagnostic for CRPS type I, however they are not entirely reliable, reproducible, easy to interpret, and they lack specificity.[98] There is also a problem of placebo effect and false-positive results. The diagnosis therefore of CRPS is one of exclusion, with these tests being used as an aid to the total clinical picture.[99] Clinical assessment remains the gold standard of diagnosis of CRPS.[100]

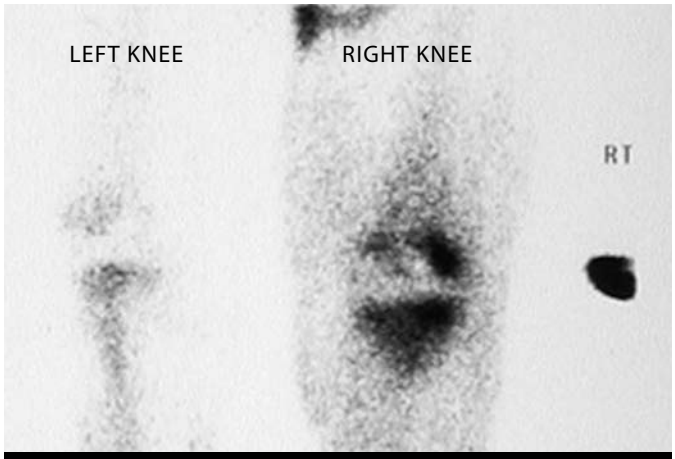


Figure 9. Bone scan of knees. In this bone scan, increased uptake can easily be seen in the right knee. This patient was diagnosed with CRPS.

The physician should take a detailed medical history considering an initial trauma and any history of sensory, autonomic and motor disturbances. The clinician should ask for the development, time course, distribution and characteristics of pain. A general neurological examination is needed. Detection of any swelling, sweating, trophic, temperature and motor abnormality in the disturbed area is important. Muscle strength of the affected limb, as well as characteristics and distribution of somatosensory abnormalities should be investigated in detail. The physician should also test whether the pain can be elicited by movements and pressure at the joints.[101] If the ligaments or soft tissues are still traumatized, stressing them by motion or pressure will elicit sharp pain. This can be documented with a dolorimeter. (*See Figure 10.*)

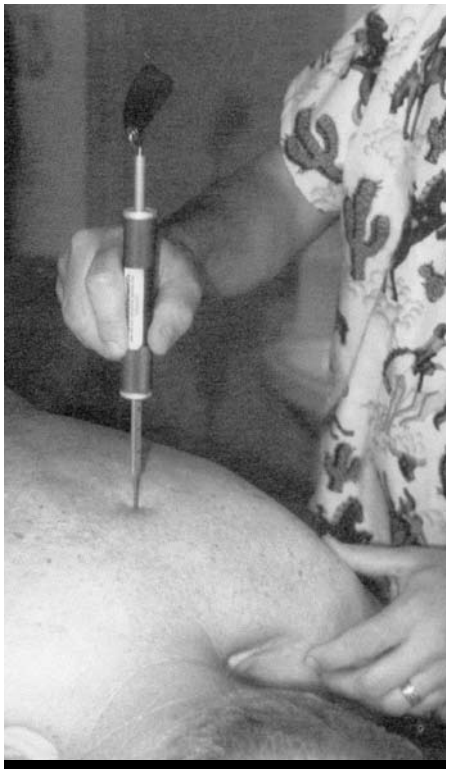


Figure 10. Dolorimeter pressure assessment. A dolorimeter measures the amount of pressure required to elicit pain at a specific location. Less pressure is needed to elicit pain at the ligaments in the CRPS patient.

Essential to the diagnosis is the presence of some initiating event and/or cause of immobilization.[102] The clinical picture includes continuing pain that is out of proportion to the event which caused it; sensory changes such as hyperesthesia; autonomic abnormalities such as changes in skin blood flow, or abnormal sweating at the site of pain, and swelling or edema which is typically peripheral, and may come and go; trophic changes of the skin and appendages; and motor dysfunction such as weakness of the muscles.[103-106] It is also necessary to exclude other conditions that may account for the pain or symptoms.

THE ROLE OF IMMOBILIZATION IN CRPS

There is strong clinical research supporting the disuse model as a basis for most of the signs and symptoms of CRPS. Most people diagnosed with CRPS have experienced an inciting injury, such as a fracture

or an identifiable soft tissue trauma with a period of immobilization or an invasive procedure requiring immobilization. The explanation that most of the signs and symptoms of CRPS may be due to immobilization has been mostly ignored.[107] The IASP diagnostic criteria itself requires the presence of an initiating noxious event, or a cause of immobilization for diagnosing CRPS. Bonica's 1953 Staging of RSD describes limitation of movement and limitation of motion as indicators of RSD.[108] Immobilization leads to both motor and sensory changes that have been the hallmark of CRPS.[109] A typical history involving a twisting injury or fracture involves casting, with the added complaint of burning pain, several more casts or walking boots may be applied for months.[110] Signs and symptoms associated with CRPS are much like those seen shortly after cast immobilization. Symptoms of prolonged casting include muscle atrophy, stiffness, skin discoloration, and often coarseness of the skin, hair, and nails.

The person with CRPS typically has intense burning pain. This pain is excruciating, whereby touching just a sheet of paper or a bed sheet to the affected limb can feel like fire. The person with CRPS learns to guard that extremity. Since movement increases the pain, those with CRPS stop moving and using their affected limbs in efforts to minimize their suffering. Many of the CRPS signs and symptoms can be produced with disuse alone, and longstanding pain from the disuse encourages further immobilization. Research has shown that this causes a sensitization of the central nervous system.[111, 112] The pain and other symptoms continue even after the original injury is healed because of the tissue changes which occurred from prolonged disuse of the limb. Most CRPS patients have reduced range of motion, however at times, passive range of motion is possible even when active range of motion is not. If the reduced range of motion was a motor function alteration then both passive and active range of motion should be affected. These deficits are thought to be due to specific alterations of central regulation of the motor functions caused by the disease. A proposed mechanism for this dysfunction is a change in the central representation induced by increased nociceptive input and by decreased sensory cutaneous and proprioceptive input due to immobilization.[113] In essence, the prolonged immobilization causes the person to be more sensitive to movement because of increased sensitivity of the small autonomic nerves.[114, 115]

Clinicians at the University of Washington Pain Center conducted a prospective study in collaboration with colleagues from Uppsala University and the Academic Hospital at Uppsala.[116] Twenty-three volunteers were casted in the non-dominant forearm for four weeks. No painful stimulus was added, since the purpose of the study was to look at immobility alone. All volunteers had temperature differences between the limbs after the casts were removed. PET (positron emission tomography) scanning showed that the immobility of the limb caused increased cerebral blood flow in areas associated with sensory processing, motor function, and emotions. Other changes caused by the immobility involved abnormal sweating, skin, hair or nail changes, hyperpathia and hypersensitivity. All of these signs and symptoms resolved following an active course of physical therapy. The researchers noted that in animal studies involving immobilization of the wrist and hind paw of rats, there was a clear demonstration of sensory changes from non-noxious to noxious findings such as thermal hyperalgesia to warmth, mechanical allodynia, and cold allodynia.[117, 118] In one study, just seven days of hind paw immobilization produced several weeks of both tactile and thermal allodynia in rats.[118] In conclusion they wrote, "It seems evident from the available data that many of the signs and symptoms of CRPS can be produced by immobilization alone…These data suggest we consider these signs and symptoms as the normal response to disuse."[119]

If disuse is primarily responsible for the signs and symptoms of CRPS, then increasing sensory input through activity and other sensory stimulation should improve the situation or at least prevent further changes.[120-122] While range of motion and physiotherapy remains one of the top priorities to prevent CRPS and to curb its symptoms, what about the person who received all of these therapies but is left with significant disabilities and pain? The question remains, if immobility is largely responsible for the chronic symptoms of CRPS/RSD is there something else that can be done to resolve the condition, once it becomes established?

LIGAMENT DAMAGE AND HEALING

As already discussed, most cases of CRPS/RSD occur after some type of trauma to bones, joints and soft tissues. One of the tissues injured in these traumas are ligaments. A ligament connects two bones and is involved in the stability of the joint. A sprain is a stretched or

injured ligament. Because ligaments generally have a poor blood supply, incomplete healing is common after injury.[123] Motion loss of the joint, connected by the ligament, is also common after injury.[124, 125] This is increased when multiple ligaments are injured, the joint is dislocated or if surgery or prolonged immobility occurs after the ligament injury.[126, 127] Prolonged immobilization has detrimental effects on periarticular cartilage, bone, and soft tissues and can lead to more motion loss.[128-130] During immobilization, connective tissues shorten, thereby further decreasing range of motion of the joint.[131] This connective tissue shortening, increases compressive forces between the articular surfaces to three times normal in just four weeks of immobilization.[132] Degenerative or osteoarthritic changes including atrophy of articular cartilage, increased fibrosis of periarticular tissues, regional bony eburnation, sclerosis and resorption can be found after only two weeks of immobilization.[133] The negative effects of periodic short-term immobilization on joints and soft tissues is cumulative.[134] In one animal study, changes in the joint and soft tissues around the joint can be seen within one week of immobilization, with marked degenerative changes appearing by four weeks. Within 80 days of immobilization, joint mobility was lost and severe destruction of the joint often followed.[135] Another study showed that even an immobilization period of four days has a cumulative effect in producing joint degeneration, and an interval of four weeks between immobilization periods does not prevent osteoarthritis from developing. In addition, this study showed that immobilization, periodic or continuous, over more than 30 days will lead to progressive joint destruction. The authors concluded that "it can be assumed that all situations which lead to the immobilization of a joint can cause osteoarthritis changes. Of interest, is that all radiology, photography, and histology showed some degree of degenerative changes also in the contralateral nonimmobilized limb."[136] Another study found that irreversible changes can occur in the joints after eight weeks of immobilization.[137]

It is easy to assume that when a person is subjected to a force significant enough to fracture a bone, that ligaments close to the fracture site would also be injured. The immobilization that follows, induces destructive changes in the joint, that itself could be painful. Once the cast is removed, for instance, the patient has numerous causes for pain including joint or muscle contractures, as well as failed ligament healing, though the fracture itself healed. Perhaps it is the failed ligament healing that is responsible for the chronic signs and symptoms of CRPS?

Ligaments are extremely sensitive to immobilization, also known as stress deprivation. Gross inspection of the ligaments after stress deprivation shows them to be less glistening and more "woody" on palpation.[138] Under a microscope the collagen of the ligament is very random and has more degradation. Chemically, the ligaments lose water and glycosaminoglycans (which help maintain structure) so there is a net loss of mass in the ligaments.[139] On close examination, it is clear that non-healed ligaments (also known as ligament scars) differ in some critical ways from normal ligament tissue. (*See Figure 11.*)

Figure 11. Differences between normal ligaments and scars.[138]

Normal Ligaments	Ligament Scars
Collagen aligned	Collagen disorganized
Collagen densely packed	Flaws between fibers
Bimodal (large) collagen fibrils	Smaller collagen fibrils
Mature collagen cross-links	Immature collagen cross-links
Primary collagen Type I	More collagen III (and others?)
Primary small proteoglycans	Large proteoglycans
Cell and matrix turnover low	Cell and matrix turnover high
Rare cell division	More cell division
Low cell density	Higher cell density
High matrix-cell ratio	Lower matrix-cell ratio

Ligament healing is a complex process similar to wound healing, but due to the poor vascularity of ligaments, the initial inflammatory phase takes longer than in wound healing.[140] Immobilization influences the appearance and biomechanical properties of ligaments, and early motion has a beneficial effect on ligament function.[141] The mechanical stress applied by the functional load with movement improves the reorientation of the collagen fiber bundles, and increases the fibril size and density. In contrast, immobilization is followed by a protracted state of catabolism within the ligament, and the degradation of the structural matrix leads to progressive atrophy and lack of mechanical strength.[142] Negative effects histologically (under a microscope) can be seen in ligaments as early as six days after immobility and proceeded destructive joint changes.[143] Other research confirms that negative structural changes in the ligaments precedes articular cartilage degeneration.[144, 145] Knee ligaments immobilized for even a few weeks showed that the ultimate load, linear stiffness, and energy-absorbing capacity of a bone-ligament-bone preparation is reduced to about one

third of normal.[146, 147] Other studies noted a decreased resistance to stretch when ligaments were subjected to immobility.[148-150] Ligaments, with their low resting blood supply, are dependent on substantial increases in blood flow and vascular volume during the initial stages of repair.[151] This healing response, however, is greatly compromised with lack of movement. Also, if the small feeder vessels are sheared during an initial injury the ligaments are unable to receive the nutritional support for healing. Effective healing responses are dependent on an adequate blood supply to provide the mediators necessary for tissue repair and to maintain joint homoeostasis during injurious episodes.[152]

Ligament injuries are very common, and they typically afflict the younger population. Ligaments in the knee and foot for instance, withstand forces of up to five times body weight which occur in each of the 1.2 million steps a person takes each year.[153, 154] While ligaments are notoriously slow healers, the repair and regeneration of the ligaments starts at 48 to 72 hours. Most ligament growth occurs between the third and sixth week after injury. One study found the maximum level of collagen in the ligament itself at six weeks.[155] Even though ligaments heal for a full year after injury, often the strength of the ligament after injury is only 50 to 70% of the original.[156] Other studies found ligaments regained only 30% of normal strength after severe injuries.[157-159]

LIGAMENT INJURY AND THE SYMPATHETIC NERVOUS SYSTEM

Ligaments have long been thought of as inert structures whose primary function is to provide stability to a joint. What has not been so appreciated is the sequelae when ligaments are injured, not just on the joint, but on the sympathetic nervous system. Non-healed ligament injuries sensitize their own nociceptors to motion. Recall that nociceptors are specialized sensory neurons (nerve cells) that respond to tissue damage. The detection of noxious chemical, thermal, and mechanical stimuli are mediated by receptors on these cells.[160] There is a high density of both myelinated and unmyelinated nociceptors in the ligaments throughout the body.[161-164] These nociceptor sympathetic nerve fibers in injured ligaments elicit pain when the ligament is under too much tension. The density and distribution of these nociceptors, also known as substance-P nerve fibers, within the ligaments is significantly affected by injury, as well as the time since injury.[165, 166] Damage done to ligaments may not initially result in a lot of pain, but the damage done to them, along with the degree of irritation on the surrounding nerve endings, may alter the firing pattern from these nerve endings in such a manner so as to cause increased activation of the sympathetic nervous system causing referral pains up and down the extremity.[167] (*See Figure 12.*) Referral pain patterns from injured ligaments is a well established phenomenon.[168-171] Ligament and other soft tissue injuries have been shown to cause regional and segmental variations in sympathetic activity including cutaneous sudomotor and vasomotor manifestations.

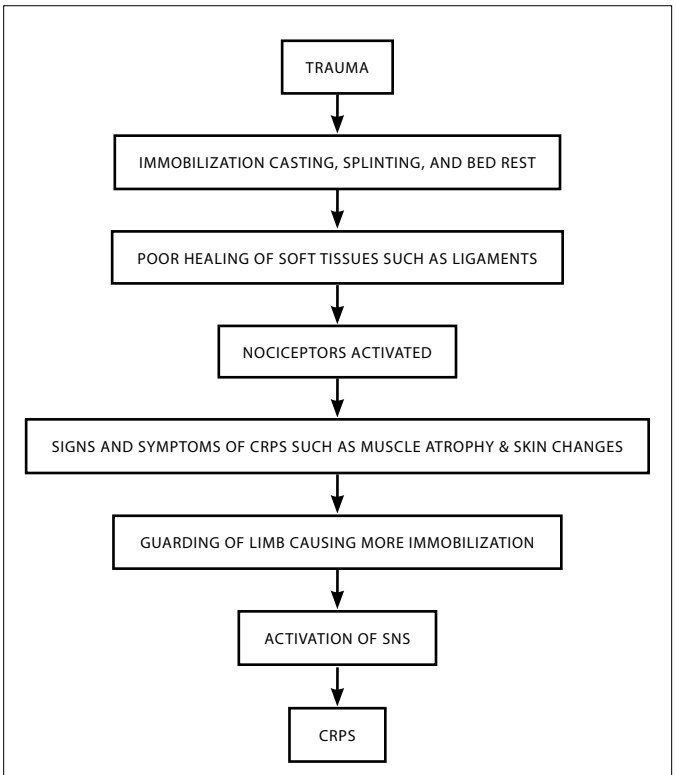


Figure 12. The non-healed ligament injury/CRPS connection. The poor healing of soft tissues, such as ligaments from immobilization, can sensitize nociceptors which ultimately can lead to CRPS.

These can include coldness and clamminess of the skin.[172, 173] For instance, when hypertonic saline (6% NaCl) is injected into the interspinous ligaments or the periosteum of the spinous processes, the local transient pain was soon followed by a crescendo of deep pain in areas often remote from the site of injection, followed by autonomic nervous system changes in the referral pain sites. The condition whereby a hyperirritable spot (myofascial trigger point) causes referral pain from that location and autonomic

phenomena is known as myofascial syndrome. The authors noted that "visceral, circulatory and thermoregulatory functions, controlled by the autonomic nervous system are continually coupled, in highly organized patterns, to musculoskeletal activity and changes in posture." They go on to say, "In these stressful and, in some cases, painful experimental situations affecting small parts of the musculoskeletal system, the afferent volleys of impulses entering through individual dorsal roots appear to have become so prepotent as to dominate that part (i.e., corresponding and neighboring segments) of the sympathetic nervous system, and to take precedence over vertically organized patterns they ordinarily serve, and even to disrupt them. They do not, therefore, meet any particular functional demand, they are not adaptive and, in many cases, they persist after the provoking insult has ended. The autonomic concomitants of local myofascial irritation, injury, stress or pathology have not received widespread recognition in clinical practice…Whether reflexly or directly provoked, the hyperactivity of isolated portions of the sympathetic outflow serves no obvious adaptive function."[174, 175] In summary, these authors found that even a small irritation of the musculoskeletal system can cause such an enormous stimulation of the sympathetic nervous system (SNS) that the pain and overstimulation of the SNS overtakes everything and it serves no useful function.

It is important to realize that the majority of cases (56% to 61%) of CRPS have a myofascial component. Myofascial dysfunction is more prevalent in the affected upper extremity (69-70%) than the lower extremity (42-47%).[176, 177] Likewise, it is known that patients with known musculoskeletal problems, including myofascial pain syndromes, have exaggerated regional sympathetic responses. When the normal limb is compared in regard to the sudomotor and vasomotor activity including edema, changes in skin floor, decreased electrical skin resistance are profoundly altered in the painful limb.[178] These heightened sympathetic responses are not anomalous reflexes, but modifications of normally operating patterns of somato-autonomic coordination that represent changes in sensory input arising in nociceptors in the injured musculoskeletal tissues.[179] Nociceptors in injured soft tissues such as joint capsules and ligaments have a lowered stimulus threshold to induce pain.[180] These nociceptors can activate the sympathetic nervous system to produce symptoms and also change blood flow to the affected joint which can affect healing.[181] In addition, joint instability caused by ligament injury, can affect the firing of nociceptors which then in turn affects proprioception (position sense) and muscle coordination.[182, 183]

According to an interdisciplinary expert panel for CRPS, the goal of treatment in patients with CRPS is to improve function, relieve pain, and achieve remission. They go on to state, "increasing evidence suggests that some cases are refractory to conservative measures and require flexible application of the various treatments…There is widespread agreement among experts that patients who do not respond to an acceptable level of treatment by 12 to 16 weeks should be given a trial of more interventional therapies…"[184] Again, to go back to the International Association for the Study of Pain Diagnostic Criteria for CRPS *one must have the presence of an initiating noxious event, or a cause of immobilization*. Surely ligaments can and probably are injured in most of the initiating noxious events that start the CRPS including the traumas that fracture bones and injure the soft tissues. As discussed, immobilization of a joint itself can cause articular cartilage and joint degeneration as well as set up a scenario whereby the soft tissue injuries including the ligaments, don't heal. Most patients with CRPS will describe weeks and even months of partial and total immobilization of the painful extremity. If underlying non-healed ligament injury is the primary causative factor for ongoing sympathetic activity, then the only treatment that would have curative effects long-term must address this issue. Most therapies offered to CRPS patients do not address ligament weakness and injury.

TREATMENT

Success in traditional treatment of CRPS is dismal. "No other chronic pain syndrome is as shrouded in confusion and controversy—to the detriment of efforts to rigorously define an evidence-based treatment strategy."[185] A study of 146 patients found that only 29% were pain free.[186] In another series, 64% of CRPS patients with severe pain lasting more than one year rated their pain as a 7 on a 1-10 scale, with 10 being the highest level of pain.[187, 188] CRPS was also noted to be present 10 years after a fracture of the distal radius in 9% of patients studied in a review of 100 patients with Colles' fracture.[189] In a Korean study involving 150 patients, one third had intractable chronic pain even after treatment, and some required a limb amputation. The Korean study noted that the patients had suffered for over two years before being referred to a specialist, and that the intractable chronic pain increases

as the time between the onset of symptoms and diagnosis increases. It is not unusual, however, that years go by before the CRPS patient even receives a correct diagnosis, thereby prolonging treatment.[190] This is possibly due to a misconception that the pain is a psychiatric disorder, or unbelief that the patient could possibly have this much pain, or even that such a small injury could lead to total body pain.[191]

Treatment is often based on the possible mechanisms that cause CRPS, however as previously noted, these causes are elusive.[192] The primary goal of treatment is to facilitate functional restoration, however, the natural history of CRPS treatment suggests that reported outcomes of pain relief, functional capacity, and disease remission are far from optimal.[193-195] Due to the historic disagreements over diagnosis of the syndrome, there are no scientifically well-established treatment guidelines. Although there are obvious difficulties in treating this disorder, there are few randomized controlled trials of the most widely accepted treatment approaches.[196-199] Clinical trials that have been performed had either small numbers of patients or limited clinical follow-up.[200] "The consensus of treatment should be to convince the patient and family that CRPS is the diagnosis and that movement of the involved extremity is key for rapid return to function."[201]

WHAT ARE THE TRADITIONAL TREATMENT OPTIONS?

Options available for CRPS include interventional, pharmacologic, physical/occupational therapy, and psychologic techniques. Staton-Hicks et al. note in their treatment guidelines that failure to achieve a favorable response with any treatment modality should not persist beyond two weeks.[202] Quisel et al. suggest these same treatment guidelines are summarized without a systematic or evidence-based approach, and also raise the question whether any treatment makes a difference, or that possibly CRPS type I resolves on its own.[203]

Interventional approaches include various sympathetic ganglion blocks (i.e., stellate, thoracic, lumbar), intravenous regional sympathetic blocks (Bier blocks), somatic blocks (i.e., peripheral nerve blocks, brachial plexus), and epidural blocks.[204]

If CRPS is a pathologic reflex of the sympathetic nerves causing blood flow irregularities, constant pain, muscle atrophy, and fibrosis, then those who support this hypothesis cite pain relief from a sympathetic block as supportive evidence. Sympathetic blocks, however, did not prove to be a reliable predictor of treatment response.[205]

The following is a note taken from a proponent of the success of the stellate ganglion block: "If the pain returns, and it does in many instances, the patient should receive a series of blocks. In the cases where the pain returns in a few hours, the first four to five blocks should be given once a day and the next three to five blocks, once every three to four days. Persistent, intensive therapy is important. If the disease is well established, the results of stellate ganglion therapy are not as promising."[206] Invasive therapies such as the sympathetic ganglion block are minimally, if at all, effective.[207]

The use of the regional sympathetic block is based on the theory that chronic pain results from either a central hyperactivity of the sympathetic nervous system or a peripheral hypersensitivity to circulating catecholamines.[208] Efficacy of these blocks in treating CRPS is unclear because separate studies dealing with similar patient populations report contradictory levels of response to treatment. Some studies show no difference between the use of the drugs and the saline control, while others report an improvement in 75% of the patients.[209, 210] In a study of the effectiveness of sympathetic blocks, one series showed only 12% of patients were pain free at a three-year follow-up.[211, 212] Only the subset of CRPS patients with sympathetically maintained pain (SMP) exhibit pain responsiveness to the blockade.[213] Many practitioners believe that some patients obtain real benefit from the sympathetic block, and other practitioners do not. Unfortunately, one cannot tell beforehand whether the patient will be one that would respond.[214]

Pharmacological approaches, including narcotic pain medications, are of little restorative value and frequently result in drug dependence without improving limb function.[215, 216] Given these limitations, treatment approaches are based heavily on clinical experience. The best treatments appear to be non-invasive and completely within the realm of family medicine.[217] (*See Figure 13.*) Guidelines help, but creativity, compassion and flexibility are essential.[218]

Early intervention is paramount. A multifaceted treatment approach is thought to be most effective. Pain management techniques to restore function are based on a steady progression from very gentle movements on an

Figure 13. Traditional treatments given to 134 patients, diagnosed with CRPS, in the Allen Study.[42]

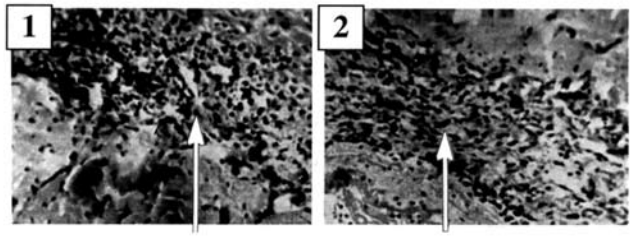
Immobilization	47%
Tricyclic antidepressants	78%
SSRI's	38%
Anticonvulsants	60%
Opiates	70%
Physical therapy	88%
Occupational therapy	45%
Nerve blocks	82%
Spinal cord stimulation	6%
Psychological treatment	50%

active basis to gentle weight bearing. This progresses to more active load bearing techniques. These strategies also include progressive stimulation using different textures and different temperatures of bath water. It is thought that this gradual normalization of sensation occurs due to a resetting of the altered central processing in the nervous system. Moving and using the limb is paramount to healing.[219-221]

PROLOTHERAPY FOR NON-HEALED LIGMENT INJURIES AND ITS ASSOCIATED AUTONOMIC PHENOMENON

George S. Hackett, M.D., a trauma surgeon at Mercy Hospital in Canton, Ohio, coined the term Prolotherapy. As he describes it, "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 and permanently eliminate the disability."[222] Dr. Hackett showed that Prolotherapy stimulated the normal inflammatory reaction by studying the effects of Prolotherapy on animal tissues. For instance, rabbit tendons injected with Prolotherapy solution examined at various intervals histologically showed an infiltration of normal inflammatory cells without any evidence of necrosis (damage) to nerves, blood vessels or tendon tissue. (*See Figure 14.*) The rabbit tendons were also noted to increase in diameter by 40% and the tendon-bone interface diameter (fibro-osseous junction) increased by 30%.[223] Dr. Hackett turned animal research into clinical application as he published numerous scientific papers advocating Prolotherapy. The main emphasis in his papers was his findings that most chronic pain was due to non-healed ligament injuries causing joint instability. Prolotherapy stimulated ligament growth and repair causing joint stabilization.[224-226] For instance, in 1955, Dr. Hackett analyzed 146 consecutive cases of undiagnosed low back disability during a two-month period. He found that 94% of the patients experienced joint ligament injury, or what he called relaxation.[227] In other words, they had non-healed ligament injuries. In 1956, a similar survey of 124 consecutive undiagnosed low back disability patients revealed that 97% of patients possessed joint instability from ligament weakness. Even though 50% had already undergone back surgery for a presumed disc problem, Prolotherapy produced cures of their low back in 80% of the cases.[228] In his largest case series involving 1,857 patients, Dr. Hackett found non-healed ligament injuries as the cause of pain in 1,583 of the cases. Follow-up on the patients 12 years after treatment found that Prolotherapy cured 82% of the patients.[229] Similar results were found when Prolotherapy was done to ligaments in the neck that caused neck pain and headaches.[230, 231] Dr. Hackett's conclusion that ligaments are a primary cause of chronic joint pain and instability that is successfully treated by Prolotherapy, has been confirmed by numerous authors for low back pain,[232-235] knee pain,[236, 237] TMJ pain,[238, 239] and many other joints.[240-245]

Dr. Hackett coined the term "ligament relaxation" to explain the weakness associated with non-healed ligament injuries. He noted, "Ligament relaxation is a condition in which the strength of the ligament fibers has become impaired so that a stretching of the fibrous strands occurs when the ligament is submitted to normal or less than normal tension."[246] When the weakened ligament is stretched, Dr. Hackett noted that it caused not only local



1. Arrow points to moderate infiltration of lymphocytes 48 hours after injection of proliferating solution. Note absence of cell-death in surrounding tissues.
2. Beginning fibroblastic organization present in adjacent tissues. Arrow points to capillary proliferation with moderate infiltration of lymphocytes. *Two weeks after injection, this microphotograph shows new tissue growth.*

Figure 14. Micrographs of sections from rabbit Achilles tendons following the injection of the proliferant, Sylnasol. The same technique was done as that which is used clinically.

pain but also referral pains throughout the body. Those referred pain patterns of ligaments were outlined in Dr. Hackett's observations after he performed more than 18,000 intraligamentous injections to 1,656 patients over a period of 19 years.[247] For instance, he found the most common cause of sciatic pain down the leg was from sacroiliac ligament relaxation.[248] He also observed that non-healed ligament injuries commonly caused bone dystrophy,[249] another term for the decalcification of bone commonly known as osteopenia or osteoporosis.

He explained in detail the pathophysiology involved, "When the ligament fibers do not regain their normal tensile strength following strain, the fibers stretch under normal tension and permit excessive tension-stimulation of the non-stretchable sensory nerve fibrils, which are abundant within the fibro-osseous attachments. This is the original of noxious barrages of sensory afferent and antidromic impulses which cause pain and bone dystrophy (decalcification). Tension stimulation on afferent sensory nerves within the weak fibro-osseous attachments of ligament to bone is the origin of barrages of afferent impulses transmitted to the spinal cord and to the brain where they are interpreted as pain and referred pain. While from the same origin, barrages of antidromic impulses pass directly and by axon reflex to bone blood vessels and cause a neurovascular disturbance of bone metabolism that results in direct decalcification, which further weakens the ligamentous attachment to bone. From the afferent stimulation in the spinal cord, there are noxious barrages of efferent impulses that cause muscle spasm, while other efferent and sympathetic impulses pass from the same and adjacent cord segments and cause a reflex neurovascular decalcification of large areas of bone. This weakens the attachment of all ligaments and tendons in the decalcified areas and completes a vicious circle of ligament relaxation and decalcification."[250] (*See Figure 15.*)

The decalcification or weakening of bone is one of the hallmark features of chronic CRPS.[251-253] Dr. Hackett showed that Prolotherapy not only could resolve the localized ligament pain, but also the autonomic nervous system phenomenon of referral pain, vasomotor changes, and bone dystrophy.[254-257] The resolution of disorders involving the autonomic nervous system including reflex sympathetic with Prolotherapy has subsequently been reported.[258-260]

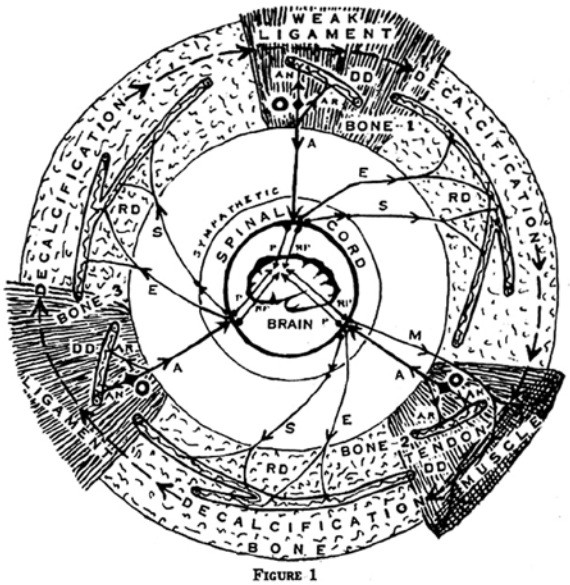


FIGURE 1

O—Origin of neural impulse by traction-stimulation of nerve fibrils within weakened fibro-osseous attachment of ligament to bone
A—Afferent sensory somatic noxious impulse to spinal cord
AR—Axon reflex neurovascular impulse in antidromic direction through afferent fibril
AN—Antidromic neurovascular impulse
DD—Direct decalcification (metabolic)
E—Efferent neurovascular impulse
S—Sympathetic neurovascular impulse
RD—Reflex decalcification (metabolic)
M—Reflex motor impulse to muscle
P—Pain impulse to brain
RP—Referred pain impulse to brain

Note: The etiology may be trauma or disease. All ligament-tendon attachments become weakened when invaded by decalcification and are the origin of most pain in all types of osteoporosis.

Figure 15. Pathophysiologic schemata connecting ligament weakness to bone decalcification.[250]

COMPLEX REGIONAL PAIN SYNDROME CASE REPORT

R.A., a 27 year-old female college student sustained a severe injury to her left foot after twisting her left ankle while out walking in the fall of 2002. X-rays revealed a metatarsal fracture in November, 2002. Initial treatment involved primarily rest and several prolonged sessions of immobilization involving the patient wearing a walking boot. She was also prescribed NSAIDs, narcotics, and received several spinal blocks because of the intense pain. She remained on these treatments for two years after the initial injury but only saw her pain increase to the point where she could not put pressure on the left foot, and was unable to walk without a crutch. She said she could not wear a sock, slept with her foot outside the covers, and even the water from a shower caused intense pain. Her studies suffered, and she needed higher and higher doses of narcotics and anti-depressant medications just to get through the day. She saw around 20 specialists during a two year span including orthopedists, podiatrists, psychiatrist

pain specialist and various therapists. In December 2004, an MRI revealed a torn tendon in the foot which was surgically repaired. Unfortunately, surgery did not help her symptoms. The severe pain and swelling in the foot and ankle increased and persisted. Treatment at this time included several rounds of steroid and trigger point injections, immobilization, more NSAIDs, immobility and physical therapy without success. In 2005, she was diagnosed with reflex sympathetic dystrophy (CRPS).

In April, 2005 she presented to Caring Medical in Oak Park, Illinois with the hopes that Prolotherapy would offer her some relief. By this time, she was on Norco® 10/325, needing 10-14 tablets per day for pain. She was seeing a psychiatrist for depression, and was taking Cymbalta® for her anxiety and depression. Aside from intense pain she had the following concerns: severe insomnia, night sweats, weight gain of over 60 pounds since her injury, fatigue, and constipation. Her initial physical exam noted a cold, swollen and discolored left foot and ankle. She had significant tenderness (evidenced by dolorimeter measurements) in the ligaments supporting primarily the lateral and medial ankle. Because of her myriad of symptoms, a comprehensive natural medicine laboratory analysis was done which revealed low testosterone and DHEA levels. Natural hormone replacement for testosterone and DHEA were then prescribed. She was also asked to change her diet as she had significant food sensitivities for dairy and moderate sensitivities to gluten and eggs. Her venous blood pH being elevated, she was started on a hypoallergenic vegetarian diet.**

Prolotherapy was started in the April 2005. Because of the severe pain in her left foot, she received conscious sedation to get through the Prolotherapy treatments. When she was seen for her third treatment in June, 2005 she was happier and reported that her standing tolerance had remarkably increased, and her pain level was down 15%. She continued to improve and was able to start wearing an electromesh sock on her left foot to help her foot tolerate more and more stimulation. The CRPS symptoms gradually improved. By the sixth visit no temperature or color asymmetry was present and the skin sensitivity significantly diminished in the left foot and ankle. By the seventh visit she was off all narcotics and antidepressant medications. Prolotherapy allowed her to finish graduate school, get married and she is now working full time as a social worker. It has been four years since her last Prolotherapy visit and she continues to live a normal, active life.

SUMMARY

To diagnose CRPS, according to the International Association for the Study of Pain Diagnostic Criteria, an initiating noxious event or a cause of immobilization must be present. Complex regional pain syndromes present as amplified somatic, motor, and sympathetic responses to injury or immobilization. CRPS is often precipitated by a deep tissue injury such as a ligament sprain or fracture. Typically, the injury is treated by casting, splinting or orthopedic surgery, which itself requires a period of immobilization. Immobilization itself has been shown to reproduce many of the symptoms of CRPS and itself can contribute to the non-healing of soft tissue injuries such as ligaments. Following trauma, ligaments show poor healing responses which themselves can contribute to a loss of motion of the joint. There is a high density of nociceptors in the ligaments of the body. These nociceptors have heightened activity to injury which can cause an exaggerated vasomotor and sudomotor response in the involved extremity, including edema, changes in skin blood flow, or decreased electrical skin resistance. Since CRPS is an extremely painful condition, patients do not move the involved extremity much. Since ligaments are very sensitive to immobilization, also called stress deprivation, they never heal, though other injuries, like bony fractures, resolve. This non-healed ligament injury continues to activate the sympathetic nervous system and the patient continues with the chronic symptoms, including the severe burning pain of CRPS. While traditional therapies such as physiotherapy, range of motion exercises, and pain medications offer temporary relief, they often do not cure the condition because they do not address the underlying ligament weakness/injury. Prolotherapy, an injection technique designed to stimulate tendon and ligament repair, has shown promise from some anecdotal reports. Prolotherapy, by stimulating ligament regeneration, not only resolves the pain, but also the sympathetic hyperactivity and the related symptoms of CRPS. Prolotherapy is a treatment that patients with CRPS and the doctors who treat them should consider. ■

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Due to the extensive bibliography of 260 references, it is available online only. Please visit www.journalofprolotherapy.com.

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WONDER WHY?

Platelet Rich Plasma Grafts In Musculoskeletal Medicine

Kristin S. Tate, MD, MPH & David M. Crane, MD

ABSTRACT

Platelet Rich Plasma (PRP) grafts are growing in popularity in the musculoskeletal arena. This article explains the risks and considerations for using PRP in the clinical setting, in addition to the authors' method of preparing a PRP graft. This article reviews the basic biology of platelets and growth factors, as well as the stages of healing. Lastly, the authors review the medical literature related to PRP and discuss their experience with PRP in their private practice.

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KEYWORDS: growth factors, platelet biology, Platelet Rich Plasma, PRP graft, ultrasound.

INTRODUCTION

The use of Platelet Rich Plasma (PRP) grafts in treating patients in the musculoskeletal arena has grown exponentially in the last few years. Since it first was introduced in 1987 by Ferrari et al in the cardiothoracic surgery arena,[1] PRP has been used and proven effective in multiple other medical specialties including cosmetic surgery, podiatry, ENT, neurosurgery, dentistry, maxillofacial surgery, urology, wound healing and ophthalmology.[2, 3] Although providers practicing musculoskeletal (MSK) medicine began using PRP for tendonosis and tendonitis in the early 1990s,[2] an informed patient population fueled by media attention has accelerated patient interest in this therapeutic alternative.

BASICS BIOLOGY OF THE PLATELET

Although this article aims to focus on clinical applications of PRP in musculoskeletal medicine, a brief discussion of blood components and growth factors is necessary. Blood is comprised of red blood cells, white blood cells, plasma, and platelets. Platelets have a lifespan of 7-10 days and aggregate at the site of an injury. The platelet is responsible for hemostasis, construction of new connective tissue, and revascularization.[4] The body's natural reparative mechanism relies on the ability to concentrate platelets and white cells within a fibrin clot at the injury site, which results in a controlled inflammatory response, predictably followed by a proliferative healing response. The proliferative healing response is dominated by platelets and white blood cells selectively time releasing growth factors, recruiting stem cells, and supporting tissue regeneration.[5]

Platelets are formed in bone marrow and contain many intracellular structures. For clinical application, the most notable of these components are two types of granules – the alpha granules and the dense granules. The alpha granules contain coagulation proteins, growth factors, cytokines, chemokines and various other proteins, including adhesion proteins. Platelets are known to contain at least six growth factors that are well known and have previously been proven to be vital to bone and soft tissue healing. *Table 1* summarizes these growth factors and their function.[2, 3] It is the rapid arrival of platelets to the area of injury and their ability to release these growth factors, that allow these tiny cells to play such a vital role in the healing process. The dense granules contain ATP, ADP, serotonin and calcium.[3] Thus, it is the dense granule that provides the factors necessary for platelet aggregation.

PLATELET ACTIVATION

It is necessary for platelets to be activated at the level of tissue injury in order for the PRP graft to be successful. It is during activation that the platelets successfully release their contents and begin the cascade of events that lead to the restoration and growth of normal collagen. The process of collagen repair can be separated into three separate phases or stages.

The three vital stages of healing are inflammation, proliferation, and remodeling.[6] All three of these stages are needed for successful return of a tissue to its

Table 1. Major growth factors in PRP and their roles.

Growth Factor	Role
Transforming Growth Factor-beta **TGF-β**	Regulates balance between fibrosis and myocyte regeneration; Stimulates undifferentiated mesenchymal cell proliferation; Regulates collagen synthesis; Stimulates angiogenesis; Stimulates endothelial chemotaxis; Inhibits macrophage proliferation; Regulates mitogenic effects of other growth factor.
Platelet Derived Growth Factor **PDGFa-b**	Stimulates cell replication; Stimulates angiogenesis; Regulates collagen synthesis; Mitogenic for fibroblast/glial/ smooth muscle cells; Mitogenetic for mesencymal cells and osteoblasts; Stimulates macrophage and neutrophil chemotaxis.
Vascular Endothelial Growth Factor **VEGF**	Stimulates angiogenesis; Increases vessel permeability; Mitogenetic for endothelial cells.
Basic Fibroblast Growth Factor **bFGF**	Stimulates angiogenesis; Stimulates proliferation of myoblasts; Mitogenic for mesenchymal cells, chondocytes and osteoblasts; Promotes growth/differentiation of chondrocytes and osteoblasts.
Epidermal Growth Factor **EGF**	Stimulates angiogenesis; Stimulates proliferation of myoblasts; Mitogenic for mesenchymal cells, chondocytes and osteoblasts; Promotes growth/differentiation of chondrocytes and osteoblasts.
Connective Tissue Growth Factor **CTGF**	Promotes angiogenesis and cartilage regeneration; Promotes fibrosis and platelet adhesion.

normal function. From the time of platelet activation the inflammatory phase begins and can last up to three days. It is during this initial phase that the all-important growth factors are released. After the inflammatory phase, the influx of fibroblasts to the area of injury mark the beginning of the proliferative phase of healing. This second phase can last for weeks, during which time the fibroblasts differentiate and neo-vascularization occurs. The final stage of healing is the remodeling phase, during which the newly laid down collagen matures and strengthens. This final phase of healing can take up to one year to complete.[2, 6]

PLATELET RICH PLASMA MATRIX GRAFTS

Crane and Everts define PRP matrix graft as a "tissue graft incorporating autologous growth factors and/or autologous undifferentiated cells in a cellular matrix whose design depends on the receptor site."[2] PRP is the therapeutic outcome of the centrifugation, or pheresis, of an autologous blood sample in order to extract that portion of the plasma that contains the highest numbers of platelets.[7]

Normal platelet concentration in the blood is 200,000 platelets/ul. PRP has been found to contain up to 10 times the concentration of platelets found in whole blood. Individual patient factors and manufacturer's equipment leads to a degree of variability in final platelet numbers seen in a PRP graft. It is accepted that a PRP graft with a platelet count five to six fold greater than baseline value appears to be adequate to achieve significant outcomes. Many manufacturers promote a high platelet concentration as a reflection of the quality of their device. It must be kept in mind that there exists some data to support that PRP grafts with platelet concentrations greater than eight fold may have pro-inflammatory effects leading to inhibition and possible negative outcomes.[8]

PRP is obtained from a sample of the patient's venous blood drawn at the time of treatment. The blood draw occurs with the addition of an anticoagulant, such as citrate dextrose A to prevent platelet activation prior to use. This sample is then placed in a specialized "table-top" device that allows for automated separation of the PRP from the PPP (platelet poor plasma) and the RBC's (Red Blood Cells). The PRP contains a thin layer of concentrated platelets and a "buffy coat" layer containing an elevated level of leukocytes. Both the concentrated platelets and the "buffy coat" are suspended in a small amount of plasma for subsequent grafting. A 60cc venous blood draw will yield from 6-10cc of PRP depending on the device used and the technique employed. (*See Figure 1.*) This PRP graft is then activated at the time of injection with the addition of calcium and thrombin or when coming in contact with collagen.

Once it has been made, the PRP graft can be placed directly into the damaged tissue to initiate and accelerate repair and regeneration. The successful placement of the

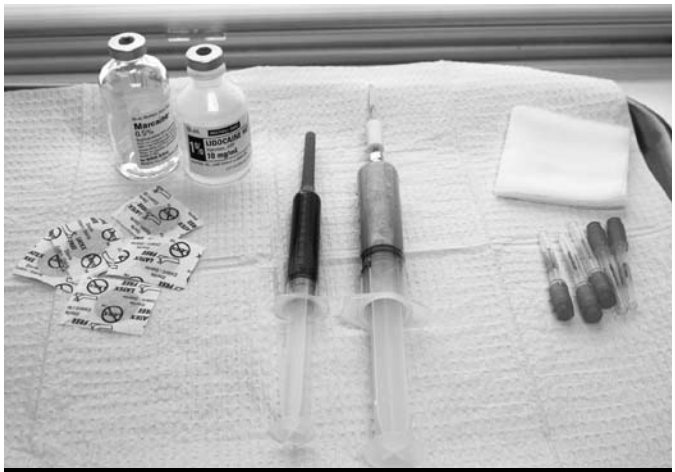

Figure 1. PRP graft ready for injection.

graft into the exact location of damage is necessary for optimal results. This application can be accomplished in the office setting by employing needle-guided radiological visualization of accurate placement (MSK ultrasound, fluoroscopy, CT, MRI), and in the operative setting via open or arthroscopic techniques.

RISKS AND CONTRAINDICATIONS

The natural acceleration of patient healing achieved with PRP has been proven to be inherently safe. The PRP graft is derived from autologous blood drawn at the time of treatment. Any allergic potential would be due to additive agents such as local anesthetics employed for patient comfort at the time of injection. Thorough screening should bring the risk of allergy effectively to zero. The autologous nature of the sample also eliminates concern over disease transfer. The application of the PRP graft should occur under sterile conditions. Under such conditions the risk of infection is the same as that of any percutaneous technique—1:50,000.[2] It has also been shown that due to the presence of white blood cells, PRP grafts are bacteriocidal, especially against Staphylococcus aureus and E. Coli.[9] Studies of autologous PRP grafts have shown no risk of carcinogenesis.

As seen with any needle-guided delivery method there is the possibility of hollow organ puncture. This risk is lessened when the practitioner utilizes and is skilled in radiologic methods of needle guidance such as MSK ultrasound or CT. The use of such guidance techniques also increases treatment success via ensuring accurate placement of the graft.

The most common patient complaint and the most notable drawback to PRP injections is their inherently painful nature. PRP injections can be painful both during the procedure itself as well as the ensuing acute inflammatory phase. The former can be minimized via appropriate local anesthetic placement prior to introduction of the graft itself. The practitioner can also mix the local anesthetic with PRP without reducing growth factor function or causing unwanted platelet activation.[10] Post-procedure discomfort can be managed with judicious use of topical ice application and analgesics (excluding NSAIDs). A narcotic analgesic is often necessary.

Also, many patients have a phobia of needles and those medical procedures that make use of percutaneous methods. This anxiety can be minimized by the use of an oral anxiolytic prior to the procedure, or conscious sedation measures for the procedure itself. These decisions must be made based on the facility where the procedure is being performed, as well as the practitioner's and patient's comfort level. It is better to address and treat the patient's fear than to risk the possibility of syncope at the time of the procedure.

Contraindications to the use of PRP grafts include septicemia, thrombocytopenia (platelet count < 105 / uL), platelet dysfunction syndrome, hypofibrinogenemia, history of a corticosteroid injection at the treatment site or systemic use of corticosteroid within two weeks of the procedure, the routine use of NSAIDs within 48 hours of the procedure, recent fever or illness, skin breakdown or rash at site of injection, history of active tumor, cancer or metastatic state, anemia (Hgb < 10 g/dL), and active infection with Pseudomonas, Enterococcus, or Klebsiella. [2, 3, 9, 11]

PRP GRAFTS AND MUSCULOSKELETAL MEDICINE

The rapid interest in PRP and its case-based success has led to widespread use of the technique in the treatment in the musculoskeletal arena. Orthopedists, physiatrists, primary care sports medicine physicians, rheumatologists, and pain management specialists are among the practitioners who are utilizing PRP grafts in their practices to manage and treat various tendon, ligament, muscle, bone, nerve, and cartilage injuries. It is important that physicians of all specialties realize the necessity of proper training in order to successfully perform PRP grafts in their practices. The practitioner must understand the science and basic cell biology of PRP since it differs greatly from other conventional treatment options. Also, the time required to train and become skilled in using a radiologic method to ensure successful percutaneous placement of the graft should not be underestimated. Again, it needs to be stressed that ensuring the exact placement of the PRP graft directly into the area injured is vital to successful outcomes. As with any emerging treatment regimen, we owe it to our patients to first understand the reason behind its use and then to become adept at performing the therapeutic technique prior to incorporating it into our practices.

PRP IN THE CLINICAL SETTING

PRP has been demonstrated for over 20 years to be a safe and effective treatment option in both human and animal studies. A plethora of animal studies have demonstrated

the effectiveness of PRP in treating injury to tendon, ligament, muscle, bone, and cartilage.[2, 3, 4, 12] As with many emerging new treatment options most of the evidence to support the use of PRP in the human musculoskeletal arena is case-based and anecdotal. Unfortunately, most human studies to date in the musculoskeletal arena are pilot studies or case reports with relatively small sample sizes. To date, very few clinical trials have been published. Despite the lack of controlled trials, the anecdotal evidence of PRP's efficacy is marked and patient satisfaction with this alternative option when faced with chronic pain or surgical intervention is high. The authors utilize PRP in the treatment of injuries to tendon, ligament, muscle, bone, nerve and joint/cartilage with great success at pain reduction and return to desired level of activity. (*See Figure 2.*)

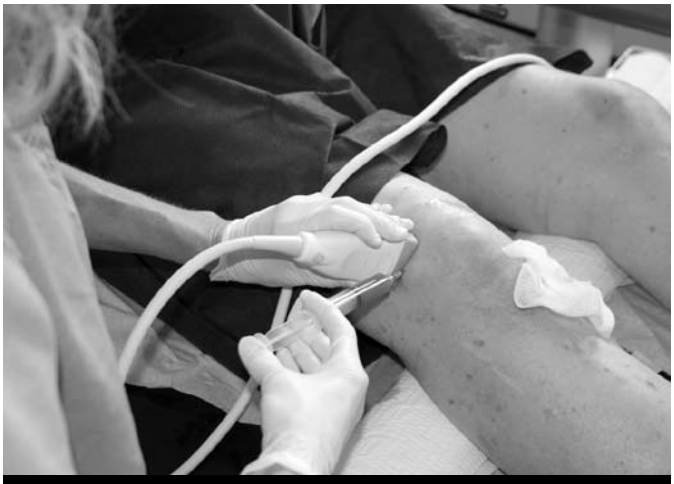

Figure 2. Dr. Tate performing PRP treatment to a knee using ultrasound guidance.

Most current published data demonstrating the effectiveness of PRP in musculoskeletal applications has been its use in tendon injury and tendon pathology. It is well accepted that tendonosis is an intrinsic degenerative disorder as evidenced by surgical biopsies. These samples show a lack of inflammatory cells and disorganize collagen matrices.[13, 14] It has also been established that chronic mechanical overuse is not the main etiologic factor in the development of tendonosis.[15, 16] A controlled, but adequate, inflammatory response followed by a proliferative healing phase is needed to treat this type of chronic tendon pathology. When directly applied to the area of tendonosis, PRP provides this exact cascade of events and leads to healing of the abnormal tendon.

A few human studies on the application of PRP on Achilles tendon rupture have been published. Sanchez[17] reported on a case control study of 12 athletes with complete Achilles tendon rupture who underwent surgical repair. The group treated with PRP had statistically significant improvement in time to functional recovery. In a follow-up report, Sanchez[18] carried out a case study of open suture repair of Achilles tendon rupture both with and without PRP. The PRP treated group recovered their range of motion (ROM) sooner, had no wound related complications, and took less time to return to running and full activities.

De Vos[19] and a group from the Netherlands recently published a study on treating Achilles tendon injury with PRP versus saline injections under ultrasound guidance. The study was a single-center randomized trial performed over a six month period on 54 subjects. The researchers concluded that among patients with chronic Achilles tendinopathy who were treated with eccentric exercises, a PRP injection compared with a saline injection did not result in greater improvement in pain and activity. This study does have some limitations. Both the PRP treatment and the placebo group underwent an eccentric exercise program. It is well known that eccentric exercise alone can lead to improved outcomes in patients with chronic Achilles tendinopathy. The study should have either included a third control group to isolate the effects of eccentric exercise or chosen only subjects who had already undergone an eccentric exercise program and failed to improve. Also, the diagnosis of tendinopathy was based upon subjective complaints and physical exam findings. If the researchers had access to ultrasound for needle guidance they should also have employed ultrasound to provide further objective evidence of chronic Achilles tendinopathy before including patients in the study group. Thirdly, there was no laboratory platelet count performed to verify that adequate concentrations of PRP were achieved prior to injection. It is well known that the concentration of platelets & leukocytes produced varies between the numerous platelet separation devices available on the market. Thus, having a known cell count is necessary in order to ensure an adequately concentrated PRP graft has been obtained. Fourthly, there was only a single injection of PRP in small amounts without noting peppering of the teno-osseous junction. In the authors' experience performing a series of two to three injections every five to six weeks provides optimum results in return to full activity without limitation or discomfort.

Looking at tendonosis in the patient with elbow pain, Mishra et al.[20] studied the use of PRP in 20 patients whose chronic (mean of 25 months) lateral epicondylitis failed surgical intervention. The treatment groups were partially randomized as follows: 15 of these patients were injected with PRP, while the remaining five received a local anesthetic. At the study's final follow-up (two years), he found a near 93% improvement in the patient's perception of pain, and that 94% had returned to full sporting or work activities. Although an excellent pilot study, the small sample size and retrospective nature of this research limits its overall power.[21]

In 2004, Barnett et al.[22] conducted a small pilot study using PRP to treat patients with plantar fasciitis diagnosed on the basis of clinical findings and confirmed with musculoskeletal ultrasound. This study was a case series of nine plantar fascia patients. All the patients underwent a diagnostic ultrasound that confirmed the presence of a thickened and hypoechoic plantar fascia. He then utilized ultrasound to inject PRP graft to both the medial and central bands of the plantar fascia. Six of nine patients had complete resolution of pain at two months and one of the three remaining patients received an additional PRP injection with subsequent symptomatic relief. At their one year follow up visit, all nine patients had ultrasound evidence of improvement in the appearance of the plantar fascia, and 77.9% of the patients were pain-free, one of whom requires a second PRP injection to reach this pain-free state.

A prospective study done by Scarpone[23] on patients with shoulder pain who had partial thickness rotator cuff tendon tears in the absence of acromioclavicular (AC) joint narrowing, was performed in 2004. The patients enrolled had all failed traditional conservative measures including NSAIDs, physical therapy and steroid injections. Twelve of 14 patients studied had statistically significant improvement in pain (using two separate pain scales), strength, and endurance at eight weeks.

Other soft tissue applications of PRP that are being used and studied are in the treatment of acute and chronic muscle tears. Sanchez[18] in 2005 published a study of 20 athletes with small intra-substance muscle tears whose underwent ultrasound guided percutaneous injection of PRP. He reported that the patients recovered up to two times faster than would be expected with other conservative treatment regimens, and none of the athletes had resultant excessive fibrosis or adverse affects.

The application of PRP intraoperatively is growing in popularity as well. Hee et al.[24] performed a controlled trial on a group of patients undergoing instrumented transforaminal lumbar interbody fusion. Twenty-three patients were randomized to the group receiving PRP intraoperatively. This study showed accelerated bony healing in the PRP group. Interestingly, there was no increase in overall fusion rate versus control.

Jenis et al.[25] studied the use of PRP in anterior interbody lumbar fusions. Twenty-two patients underwent iliac crest bone autographs and 15 received PRP and an allograft. Radiographic evaluation at six, 12, 24 months demonstrated an 85% fusion rate for the autograft group and an 89% fusion rate for the PRP plus allograft group.

Gardner[26] performed a retrospective case series in a group of patients undergoing total knee arthroplasty (TKA) who received platelet gel intraoperatively. He found that these patients that were treated with platelet gel at the time of surgery had a lower blood loss, improved ROM and less need for narcotic pain control.

Everts et al.[27] also studied the use of PRP in patients undergoing total knee replacement. This study was controlled and involved 160 patients. Eighty-five of these patients were treated intraoperatively with platelet gel/fibrin sealants. This group of patients who received the autologous platelet product had a lower post-op wound complication rate, reduced need for blood transfusion, fewer post-procedure wound infections and shorter overall hospital stays.

CONCLUSION

In summary, for over 20 years, PRP has been used safely in many medical specialties and in numerous dental applications. PRP matrix grafts are rapidly gaining popularity in the management of patients with musculoskeletal complaints driven by consumer demand and physician interest. These autologous grafts have been proven in many studies to be very safe. In the musculoskeletal arena, PRP has a host of anecdotal evidence of efficacy, and a few studies performed to date support these practice based findings. In addition, this biological alternative is a relatively low cost option to patients with a variety of tendon, ligament, bone, nerve, cartilage, and muscle pathology.

First line treatment methods such as rest, bracing or kinesiotaping, evaluation of kinetic chain abnormalities and physical therapy should be considered before pursuing the application of a PRP graft. Should these first line treatments fail, application of a PRP graft should be considered and discussion of this alternative approach needs to be shared with the patient. Once the PRP has successfully turned off the pain generators, restoration of the normal kinetic chain via physical therapy, Pilates therapy, etc…can be pursued.

The authors have been using PRP grafts in the outpatient setting with great success over the past five years. Despite such anecdotal success, there exists a desperate need for randomized placebo controlled trials to support the clinical evidence put forth in the literature to date. We have also begun using other biologic treatment options such as bone marrow aspirate stem cell grafts and other autologous matrices for those cases where a greater autologous stem cell load is needed. Future studies using validated clinical measures, and radiological, biomechanical and tissue injury/healing-responsive biomarkers as secondary outcome measures are needed to determine whether PRP and other autologous biologic grafts can play a definitive role in a cure for musculoskeletal injuries. ■

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WONDER WHY?

Effective Treatment of Chronic Pain by the Integration of Neural Therapy and Prolotherapy

Gerald R. Harris, DO

ABSTRACT

Chronic pain is a major problem in our society. Neural Therapy , like Prolotherapy, is an injection method of healing. Developed in the early 1900s by Ferdinand and Walter Huneke, Neural Therapy is one of the best known natural healing methods in Germany, and is now also practiced in Europe and the U.S.. Neural Therapy is designed to repair and restore normal function to the Autonomic Nervous System (ANS), that part of the nervous system responsible for the "automatic" functions of the body such as immune function, circulation, and the production of hormones. As early as 1905, researchers noted that illness and dysfunction are almost always preceded by a dysfunction of the ANS. Neural Therapy, when correctly done, repairs ANS dysfunction, restoring the body's healing capacity, allowing Prolotherapy, if still needed, to work more effectively. This article explores the history and science behind this fascinating treatment.

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KEYWORDS: ANS, autonomic nervous system, chronic pain treatment, Huneke, musculoskeletal pain, neural therapy, Prolotherapy, regional pain syndrome.

INTRODUCTION

Chronic pain, especially musculoskeletal pain, is a major problem in our society.[1-4] The annual cost of chronic pain in the United States, including healthcare expenses, lost income, and lost productivity, for low back pain alone is estimated to be $85.9 billion,[5] with arthritis costing $128 billion.[6] In fact, pain is the second leading cause of medically related work absenteeism, resulting in more than 50 million lost workdays each year,[7] with headache, arthritis, back pain and other musculoskeletal conditions costing $61.2 billion per year.[8] It is a major problem not just because of its prevalence, but also because of the general lack of effective treatment for patients afflicted with chronic pain.[9-11] When I was in medical school learning how to treat these patients, diagnosis and treatment was reduced to an algorithm or "recipe." These formulas supposedly guide the doctor through the proper diagnosis and treatment of various pain complaints. I dutifully memorized these algorithms and when I began practice, I applied them just as I was taught. The problem is that they do not work most of the time. I would go through the algorithm as I had been taught, but most of the time the patient would be only slightly improved, if at all, and sometimes they would even get worse! I began to realize that what I had learned was at best incomplete, and at worst, wrong. I then began a long quest for more knowledge by attending numerous conferences, seminars and workshops all over the country that had to do with pain treatment. Some of these techniques were as ineffective as the algorithms, or worse. Some techniques worked, but were very labor intensive and inefficient, but occasionally I encountered information that was stellar. I have woven these different stellar techniques into a treatment protocol, which I have found in my practice to be much more effective in permanently resolving chronic pain problems. Two of the most effective treatments I found were Prolotherapy and Neural Therapy. When used together, Prolotherapy and Neural Therapy are incredibly effective in resolving even the most complex pain issues.

WHAT IS NEURAL THERAPY?

Neural Therapy, like Prolotherapy, is an injection treatment that stimulates healing.[12] Neural Therapy is one of the best-known natural healing methods in Germany and is now also practiced in other countries in Europe and the United States. Neural Therapy is designed to repair dysfunction of the autonomic nervous system, that part of the nervous system responsible for the "automatic" functions of the body, including the immune system, circulation, hormone release, and thus healing ability. Ricter, a German scientist, did animal experiments to study the relationship between the nervous system, circulation, and healing, and noted in 1905 the profound and senior influence of the autonomic nervous system. He concluded that illness and dysfunction, were always preceded by a disturbance of the autonomic nervous system, which disturbance then adversely affected the circulation to the particular tissue, limiting healing and predisposing the individual to the problem.[13] This is especially important in the musculoskeletal system since

proper blood supply to injury is so important in healing.[14, 15] An example would be if there was an injury to the autonomic nervous system that caused it to restrict blood flow to the low back, then day to day healing of that area would be diminished. Normal "wear and tear" which should heal, doesn't, and eventually that individual could develop back pain that did not resolve. Prolotherapy could, of course, help the injured ligaments and tendons, but if blood flow is poor because of that prior injury and damage to the lumbar nerve plexus, Prolotherapy treatment might be slow or reach a point and plateau, or not work at all, until that blood flow was restored with correctly placed Neural Therapy injections.

HISTORY OF NEURAL THERAPY

Two German physicians practicing in the early 1900s, Ferdinand and Walter Huneke, are considered the founders of Neural Therapy.[16] Neural Therapy evolved and developed along with the discovery of local anesthetics. The first local anesthetic, cocaine, was discovered to have anesthetic effects by the famous Sigmund Freud. Dr. Freud shared his knowledge with his friend ophthalmologist Koller, who was the first physician to perform eye surgery using a cocaine solution in 1884.[17] Because of the addictive and toxic qualities of cocaine, a search for a safer local anesthetic ensued and resulted in the discovery of procaine (introduced under the trade name "Novocain") in 1905 by Einhorn.[18] In 1906, Spiess and Schleich discovered that infiltration of procaine into a wound greatly enhanced healing. This healing lasted much longer than the duration of action of the actual anesthesia.[19] In 1925, the great French surgeon, Leiche, was the first to successfully treat a migraine headache with a local anesthetic nerve block injection and observed healing reactions produced by local anesthetics administered before an operation, sometimes avoiding the need for that surgery.[20] Leiche called procaine (a local anesthetic) "the surgeon's bloodless knife."[21]

In 1925, the brothers Dr. Ferdinand and Walter Huneke, both sons and grandsons of physicians, without any prior knowledge of the work of Spiess, Schleich or Leriche, discovered the healing aspects of procaine. This occurred by accident when, in 1925, Ferdinand Huneke gave his nurse, who he had been treating for rheumatism, an infusion of procaine and her previously therapy-resistant migraines disappeared. This "lightening reaction" impressed Dr. Huneke and he realized he may have found a new therapy for pain. He named this new therapy "Healing Anesthetics."

Neural Therapy involves the injection of local anesthetics into scars, peripheral nerves, autonomic ganglia (deep grouping of nerves), glands, acupuncture points, trigger points, and other tissues.[22] Ferdinand Huneke, along with his brother, Walter, first reported the results of their research into the healing properties of local anesthetics with the publication of "Unknown Distant Effects of the Local Anesthesia" in 1928.[23] The Hunekes reported that reaction to the injections could help organs at a distant site and described this phenomenon as a reflex. It has been stated that "a correctly applied Neural Therapy injection can often instantly and permanently resolve chronic long-standing illness and chronic pain."[24] While usually more than one injection is needed to this end, this instance of a "lightening reaction" has been noted by researchers and physicians over the years.[25]

THE AUTONOMIC NERVOUS SYSTEM

Another way to understand why Neural Therapy can have such a profound effect is to understand how the autonomic nervous system is "wired." The autonomic (involuntary) portion of the nervous system regulates internal body functions such as blood pressure and circulation, digestion, body temperature, heart rate, breathing, and affects all the internal organs, without a person's conscious effort. It is always working to maintain normal internal organ functions. In times of danger it gives the "fight or flight" response, and in nonstressful times it will "rest and digest". (*See Figure 1.*) As you can see in *Figure 1*, the autonomic nervous system is divided into two sections sympathetic and parasympathetic, both of which work on a "subconscious level" to affect the function of organs including the blood vessels, stomach, liver, kidneys, bladder, genitals, lungs, pupils and muscles of the eye, heart and digestion. If the autonomic nervous system is not functioning correctly, the health of the individual may be affected adversely.[26] For example, if suddenly a person all alone in their house on a dark, dreary evening, hears a prowler entering through a window, the sympathetic portion of their autonomic nervous system feeding into their adrenal gland dumps a load of adrenalin into that person's blood stream and he or she feels fear, agitation and heightened awareness to protect themselves. If this person lives in Texas, they will likely go for one of their weapons. If he or she lives in California, they will run to their phone and dial 911. Either way, the person is able to react and protect themselves because the input from the autonomic nervous system to their adrenal gland is functioning correctly. Imagine if the signal to the adrenal

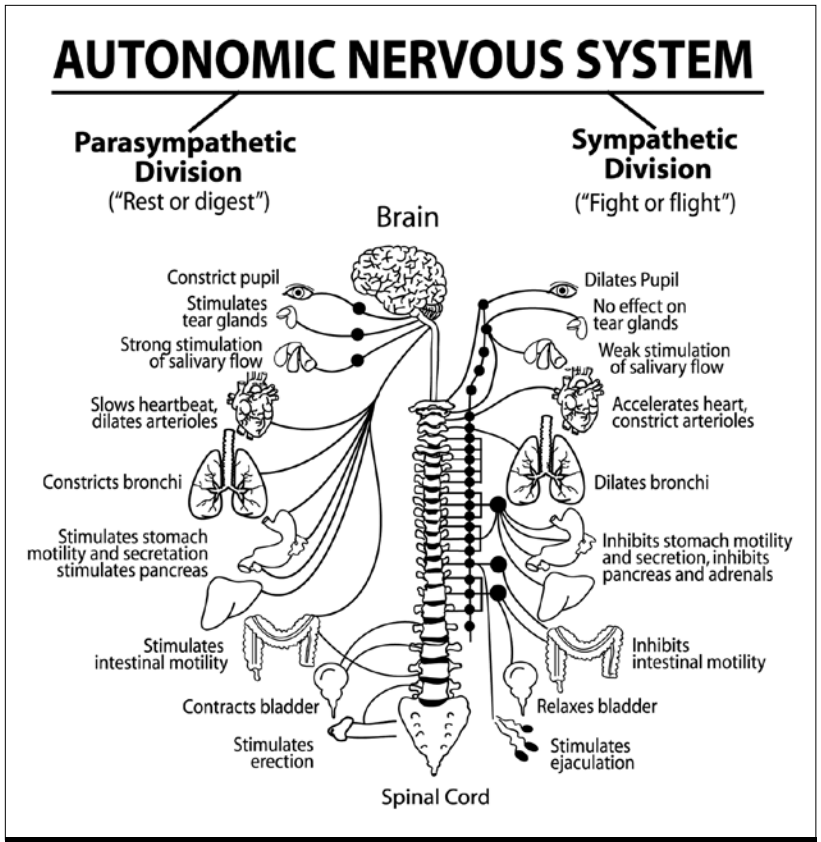

Figure 1. The autonomic nervous system.

gland wasn't working, and no input went to the adrenal gland. Then instead of reacting, the person just ignored the sound, and the prowler entered and harmed them. Or if the autonomic nervous system was too sensitized, then even the mild sound of wind blowing outside might send a person for their gun, putting them in a position to accidently hurt someone. You get the idea. We need our autonomic (automatic) nervous system working correctly to protect us and allow normal function and adequate healing. Another interesting fact is that nerve pathways often supply distant organs or locations, as seen in *Figure 1*, so a correctly placed Neural Therapy injection can have benefits distant to the site where the injection is made.[27]

HOW NEURAL THERAPY WORKS

Neural Therapy is based on the theory that any trauma, infection, or surgery can damage a portion of the autonomic nervous system and produce long-standing disturbances in the electrochemical or electromagnetic functions of these tissues.[28] These disturbances are also known as "interference fields" because they interfere with normal function and healing. When these "interference fields" persist and the autonomic nervous system is injured or not functioning correctly, various consequences can result such as incomplete healing,[29] including incomplete healing of soft tissue injuries and chronic pain. In my experience, these interference fields and resulting dysfunction can last indefinitely unless repaired.

The theory of how it works is quite interesting and logical. Local anesthetics reversibly block pain and other sensory input.[30] In the case of Neural Therapy, when correctly placed injections are done, the therapeutic effect always goes far beyond the short-term anesthetic effect.[31] This observation leads to the conclusion that anesthesia of pathologically disturbed tissue is able to induce a lasting change of nerve function towards normality, and that there is a basic difference between simple anesthesia and the neural-therapeutic effect.[32]

Recall from basic physiology how a nerve cell functions: there is a membrane resting potential (MRP) for nerve cells. This is the electrical potential (how much potential energy) a cell has when they are resting (not firing off signals). For a healthy nerve cell it is -90 mV. If the cells are stimulated (i.e. person falls, a needle goes through them, etc.), the nerve cell will lose some of its potential energy and the resting membrane potential will increase. Somewhere between –50 and –70mV a threshold is passed and the cell fires off a pain signal ("action potential"). After the stimulus is gone, a healthy nerve cell returns to its former level of -90 mV.[33] An unhealthy cell, however, will chronically be starting at a lower membrane resting potential, for instance –60 (instead of -90), and therefore a weaker stimulus (less input) would cause the cell to pass the threshold and fire a painful action potential. (*See Figure 2.*) Research done by Steinhaeusler showed that there is a difference in the MRP of cells, depending on their level of health, with unhealthy or ill cells having a higher MRP which is closer to the threshold of firing.[34] In this condition, a person would experience chronic pain because their nerve cells would be firing off pain signals with very little stimulus. The temporary introduction of the local anesthetic raises the membrane potential threshold of that cell. That is why the area goes numb and the person cannot perceive pain input for that short time. But during the

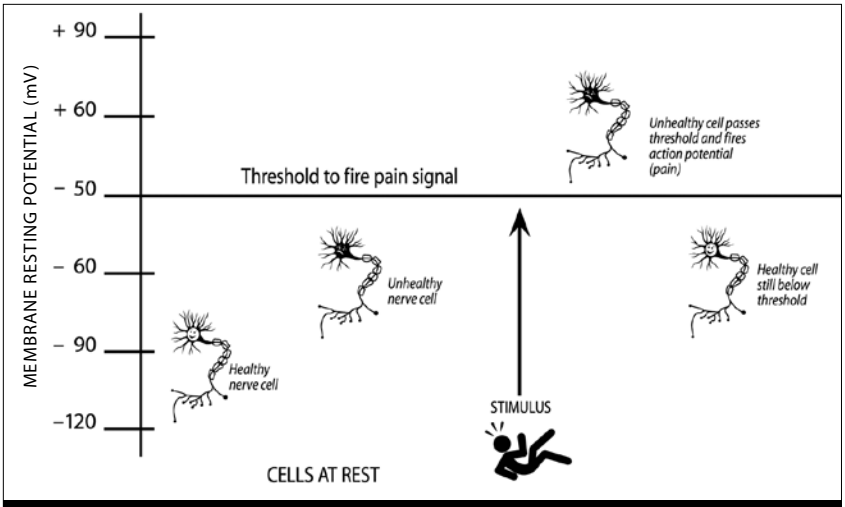

Figure 2. Healthy versus unhealthy nerve cell membrane resting potential and what happens when stimulated.

time when pain input is blocked, the cell has increased membrane potential (more energy given to it), thus the cell has improved metabolism and the sick cell succeeds (hopefully) during this time of getting rid of metabolic waste and toxins, allowing the previously sick cells to shift back towards normality.[35] (*See Figure 3.*) This can happen instantly with one treatment (lightening reaction), or more commonly after a series of treatments, each treatment restoring the regulating function as far as possible, and with each repetition allowing the cell to increasingly build up its energy potential.[36] Doing the injection in the correct site is important because this neural-therapeutic normalizing effect upon the autonomic nervous system can only be produced if the injection reaches previously damaged tissue that can no longer recover by its own efforts.[37]

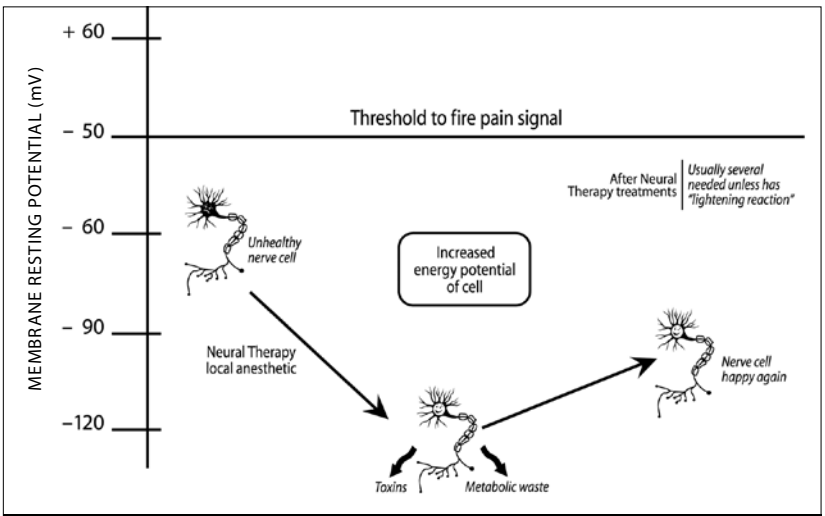

Figure 3. Proposed mechanism of how Neural Therapy helps sick cells heal.

INTERFERENCE FIELDS

A very important part of Neural Therapy treatment is the identification and treatment of "interference fields." Interference fields are areas where the autonomic nervous system is functioning below par. These fields thus "interfere" with optimum healing. Interference fields can be found almost anywhere in the body and are often far from the part of the body that is experiencing symptoms. Typical locations include scars of all types (trauma, surgical), deep autonomic ganglia (grouping of nerves) and internal organs. An interference field has also been defined as local tissue irritation with the potential to cause destabilization of the autonomic nervous system (ANS) either locally or systemically. Interference fields generally arise in locations where there has been an injury, either from sharp or blunt trauma, local infection or inflammation, or mechanical strain injury, dental work, a gland, and frequently surgical scars.[38] (*See Figures 4 & 5.*)

There is also the phenomena of interference fields affecting areas at a distance. This was demonstrated when in 1940, Ferdinand Huneke injected procaine into the shoulder of a patient with a severe and therapy-resistant frozen shoulder. No immediate relief was noted by the patient however several days after the shoulder injection the patient developed severe itching in a scar on her leg. That itching scar was injected and within seconds the patient obtained full, painless range of motion in the previously frozen shoulder. Review of history revealed the patient had previous surgery on that leg because of osteomyelitis. The surgery had been considered successful, but shortly after the surgery the patient had developed the frozen shoulder. Huneke recognized the therapeutic importance of this "lightening reaction,"[39, 40] with the scar on the leg being the site of the actual interference field.

HOW TO LOCATE INTERFERENCE FIELDS

There are several different approaches the doctor can use in the identification of interference fields. One is by history of

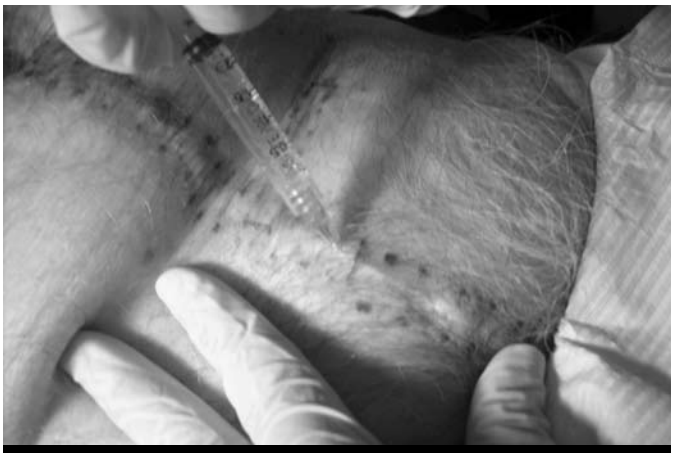

Figure 4. Neural Therapy of a surgical scar.

Figure 5. Neural Therapy of sphenopalatine ganglion by Jurgen Huneke, MD, of Germany, at Neural Therapy conference.

trauma, and correlation of symptoms to that trauma. There is the empirical method: treating all trauma sites and watching for the result. There is the proximity method: treating scars and trauma sites that are situated in close proximity to the areas of symptoms as those are more likely causative (but not always). Another popular method is Autonomic Response Testing (ART). Based on applied kinesiology, ART, when properly done, appears to be the most accurate method to detect interference fields. ART is based on the theory that a muscle will become weak when an interference field is palpated. While the actual "how" of ART still remains controversial, an individual who is tested and treated based on the interference fields located by this method, often gets well. Several studies have documented the accuracy of this method, without explaining the how.[41-43]

TREATMENT FORMULAS AND CHOICE OF LOCAL ANESTHETIC

Neural Therapy is performed with local anesthetics, usually procaine or lidocaine, and occasionally carbocaine if allergy problems are encountered. These anesthetics should **never** contain epinephrine. The standard solution I use for superficial infiltration (scars) is 1% procaine or 1% lidocaine with a small amount of sodium bicarbonate to buffer the pH and decrease the pain of the injection, although the sodium bicarbonate is optional. I will generally do autonomic response testing to determine whether lidocaine or procaine is the best anesthetic for a particular patient. Much of the early research by Huneke and others was done using procaine because it was the first local anesthetic discovered. Either procaine, lidocaine or carbocaine are considered appropriate local anesthetics for Neural Therapy treatment.[44] Lidocaine was first synthesized in 1943 by Swedish chemist Nils Lofgren, but not marketed until 1949,[45] so Procaine is sometimes favored by the Germans because historically it has been used the most. It also biodegrades into PABA, a naturally occurring and needed B vitamin. However, it is also more prone to allergic reaction than lidocaine.[46] The choice of the local anesthetic is thereby personal to the practitioner. Whichever anesthetic is chosen, however, the practitioner should take care not to exceed the maximum dose per procedure, for lidocaine: 4.5 mg/kg not to exceed 300 mg, for procaine: 7 mg/kg not to exceed 350-600 mg; and for carbocaine: 7 mg/kg not to exceed 400 mg.[47]

CONDITIONS APPROPRIATE FOR TREATMENT WITH NEURAL THERAPY

In Dosch's textbook on Neural Therapy, there is a long list of conditions and indications for Neural Therapy.[48] This makes sense because of the underlying nature of the autonomic nervous system. Of particular interest to me is the use of Neural Therapy in chronic pain and in normalizing and restoring the musculoskeletal system. I have found it helpful for any type of chronic musculoskeletal pain not responsive to other treatments, including low back pain, neck pain, headaches, and any other joint pain. Painful, sensitive or keloided scars are particularly responsive. Chronic pelvic pain is frequently responsive to Neural Therapy, as are dysmenorrhea and menstrual irregulatories. What are deemed "regional pain syndromes" are frequently secondary to autonomic dysfunction and amenable to treatment with

Neural Therapy if initiated soon enough. Trigeminal neuralgia can often be effectively treated if combined with treatment of dental infections, Raynaud's will also frequently respond to Neural Therapy. There are also references to these conditions as appropriate for Neural Therapy in Dosch's text, where he goes in detail and offers his personal experience using specific protocols for each condition.[49]

Jurgen Huneke, MD, nephew of Ferdinand and Walter Huneke, and president of the International Association for Neural Therapy, spoke and demonstrated at the 1999 Caring Medical conference on Neural Therapy. (*See Figure 6.*) Dr. Huneke summarized a list of conditions for which he considers Neural Therapy useful:

1. Acute and chronic pain (including headaches of different origins)
2. Inflammatory responses
3. Poor circulation
4. Multiple chronic conditions, caused by interrupted interference fields (such as rheumatism)
5. Diseases of the motor system (sciatica, arthritic joint conditions, shoulder or arm syndrome)
6. Internal diseases such as prostate, female, allergies, kidney
7. Sports injuries where it assists in healing.[50]

SEQUENCING OF TREATMENT: THE THREE LAYERS OF MUSCULOSKELETAL PAIN

So we have Neural Therapy, and we have Prolotherapy. Where should the doctor start in his/her treatment? To understand that answer, I will explain how I developed my own treatment protocol. After years of study and treatment of patients, I concluded that there are three layers of musculoskeletal pain.

First Layer: The first layer is that of muscle spasms. The important thing to remember about muscle spasms is that they are usually only a symptom, not a problem in and of themselves. When the body is injured or unstable, it will tighten the muscles around the unstable, weak or injured area in an attempt to stabilize it. Unfortunately, the muscles are not designed to remain in a constant state of contraction for prolonged periods. They are designed to flex and relax as one goes about daily activities. When the muscles are tightly contracted for prolonged periods, waste products such as lactic acid start to accumulate in the muscle and they will begin to cramp and hurt. So, other than the fact that the muscle spasms indicate areas where the body is detecting something wrong, I generally do not waste too much time on them to begin with as they will usually resolve spontaneously once the underlying problem is treated.

Figure 6. Jurgen Huneke, president of the International Association for Neural Therapy, demonstrating injection of the inferior hypogastric plexus at a Neural Therapy conference.

Second Layer: The second layer below muscle spasms, and the first layer where you have real pathology, is the connective tissue layer. Connective tissue refers to ligaments, tendons, and fascia. Basically, the "gristle" that holds the body together. The connective tissue is tough and difficult to damage; however, once it is damaged, it heals slowly during a window period of four to six weeks, and often does not heal 100%.[51, 52] Incomplete healing is common in the ligament and tendon connective tissue and makes the area prone to re-injury. Injured connective tissue also frequently refers pain so that often times where one feels the pain is not where the problem originates.[53] For example, a problem in the lumbar spine can cause sciatica pain down the leg, or a problem in the upper cervical can refer into the head causing headaches. So it is important to do a good musculoskeletal and connective tissue exam and history, as well as have an understanding of ligament and tendon referral patterns which can be found in several books and texts discussing this issue.[54-56]

Third Layer: The bottom layer of the three is the layer of autonomic nervous system (ANS) dysfunction. Once the ANS is disrupted, from whatever cause, there are several effects that result. One is pain. Pain from the ANS can go on as long as the dysfunction persists. My record

so far is 60 years in one patient. The second effect of ANS dysfunction is that function is altered, usually in respect to decreased blood flow to the area of the body that is controlled by that part of the ANS. This causes chronic under-nourishment of the affected body tissues, and results in progressive weakness, especially in connective tissue. The third effect of ANS dysfunction is tightening of the connective tissue around the area of ANS dysfunction. This is significant because although the connective tissue will bend and twist easily, it does not stretch much at all. Since the connective tissue cannot stretch and absorb this pull, it will transfer the force down its entire length to whatever bone it connects to. This results in restrictions or tightness in certain ranges of motion, and if present long enough or if the patient sustains some sort of high-energy trauma, it can cause the connective tissue to begin to tear loose from the bone. This will then result in a "second layer" (connective tissue) problem.

So how does the doctor chose which treatment to start with? In my practice I start at the "third layer" (ANS) and work up. I first check and repair ANS dysfunction with Neural Therapy, then any connective tissue weakness or instability with Prolotherapy, followed by physical therapy to rehabilitate the muscles. While I practice in this order, other orders of treatment can also be effective. For instance, treating a straight forward soft tissue injury with Prolotherapy first. However, if healing with Prolotherapy injections is slow or pain remains, then this is an indication that an underlying autonomic nervous system issue is present and that Neural Therapy would be appropriate.

Once the ANS dysfunction is corrected usually a large percentage of the patient's pain will subside, and sometimes virtually all their pain will be gone. In many cases, however, the connective tissue damage will be so bad that even with normal ANS function the body is unable to completely repair it. In these cases we move up to the next level of treatment, the connective tissue layer. Connective tissue damage is treated with Prolotherapy.

Once the patient's pain level has decreased to low levels from either the Neural and/or Prolotherapy, then the patient is placed into a progressive physical therapy and rehabilitation program. This reconditioning is essential to prevent re-injury, because the patient's body is usually very weak and deconditioned because of their restricted physical activity and inability to exercise.

EMOTIONAL RELEASE

A phenomena well recognized by the Neural Therapy practitioner is emotional release after Neural Therapy injections which is typically unpleasant emotions associated with the trauma sites being injected.[57] This release can start during a treatment and last for a few days afterwards, or may not occur at all. Warning the patient of this occurrence is usually sufficient to prevent misinterpretation of this expected phenomena or the patient assigning these unpleasant emotions to something in the patient's current environment.

CONTRAINDICATIONS TO NEURAL THERAPY

Absolute: Neural Therapy injections are not done into an area where there is an active cancer or active infection.

Relative: Disease states resulting from severe nutritional deficiencies or genetic illness because it will not help. Unstable diabetes, because it can cause instability in blood sugar. Of course, pregnancy anywhere near the uterus, because of possibly triggering a miscarriage. Also, severe psychological disorders are a relative contraindication because the emotional releases can destabilize the psychological state.

WHERE TO GET TRAINING IN NEURAL THERAPY

Training for doctors is available through the American College of Osteopathic Sclerotherapeutic Pain Management, a group which teaches both Prolotherapy and Neural Therapy. I routinely lecture at the ACOSPM spring conference (check www.acospm.com for details). Workshops specific to Neural Therapy and Autonomic Response Testing are also given by Dietrich Klinghardt, MD, PhD, of the American Academy of Neural Therapy, www.klinghardtacademy.com. Other workshops and seminars are given by Dr. Robert Kidd, www.neuraltherapybook.com. Dr. Kidd has also written a book on the subject available on the website.

CONCLUSION AND CASE REPORTS

The effective treatment of chronic pain can be a challenging, but rewarding, activity. The pain practitioner is advised to become proficient in any treatment which may help him/her interpret and treat even the most difficult patients. Neural Therapy, when needed, can be integrated with Prolotherapy. This combination can be

very effective in the treatment of chronic musculoskeletal pain because it increases healing capacity and allows Prolotherapy to work even more effectively.

CASE REPORT 1

71 year-old male who presented with a chief complaint of low back pain for 46 years. His first episode at age 25 was sudden onset treated with bed rest and chiropractic. The episodes continued to occur four to five times per year, and increased in duration and frequency until they were virtually continuous. Eventually, the patient received a surgical consult, told there was no surgical pathology and sent for physical therapy which provided little benefit. At the time he was seen at my office he had continuous low back pain, only varying in intensity. His only surgical history was ganglion cyst removal on his left wrist, surgery on his right wrist for unknown reasons, removal of a calcified saliva gland with complications of a "numb spot" on his lower lip that was slowly improving, as well as two wisdom teeth removals in his 20's and multiple root canals. Autonomic response testing was done and the patient was found to have interference fields at the wrist scars bilaterally, at the inferior hypogastric plexus, and inferior cervical plexus. Testing also revealed a correlation between the inferior hypogastric plexus, the right wrist scar, and his low back pain. Treatment was initiated with Neural Therapy to all found interference fields. The patient returned three weeks later for follow-up and reported significant improvement in his low back pain. The patient was treated three more times with Neural Therapy at two to three week intervals before Autonomic Response Testing revealed all interference fields to be resolved. At this point, the patient stated that his pain was occasionally gone, but that he had some intermittent areas in his low back which still caused pain. Prolotherapy was then commenced. A total of four Prolotherapy treatments were done at three to four week intervals. When the patient presented for his last treatment four months after his first visit, he stated that he had no more noticeable pain at all. He was discharged from treatment.

CASE REPORT 2

35 year-old female with history of low back pain for 10 years following a motor vehicle accident. Chiropractic adjustments did not resolve the pain and, in fact, aggravated it. The patient was also diagnosed with cervical cancer and had a complete hysterectomy approximately five years ago. At that time lymph node resection done on her right side removed 20 inguinal lymph nodes and left the patient with loss of feeling and numbness in her right pubic area and right side of thigh. After healing from surgery, the patient suffered musculoskeletal low back pain and leg pain. A lumbar spine MRI was negative for radiculopathy. The patient received several Prolotherapy treatments which gave her 75% improvement, as well as a Platelet Rich Plasma (PRP) injection treatment which gave her much more strength and further reduction of pain to 90%. This intense improvement lasted six months after which improvement went back to 75-80%, with low back pain after certain types of physical activity. During this time, the patient went on a hiking trip and hit her head on the inside of a camper shell, after which she was diagnosed with facial neuralgia and had recurrent episodes of burning facial pain, only partially helped with Neurontin. When seen at the time of her first Neural Therapy evaluation, patient was still improved in her low back (75% overall) but was getting recurrent flares of low back, and still suffering almost constant episodes of intense neuralgia facial pain. Autonomic Response Testing was positive for interference fields in the patient's upper molars, inferior hypogastric plexis, the hysterectomy and left knee scars, and the tattoo on the patient's low back. These regions were then treated with 1% procaine. The patient had good pain relief, and almost complete resolution of her facial neuralgia pain, as well as emotional release manifested in unexplained episodes of grief during the week following her first treatment. The second treatment addressed these similar areas as well as adding the hypogastric nerve plexus. The patient then had complete relief of her facial neuralgia pain, but low back pain remained. For the third treatment, Autonomic

Dr. Harris performing an inferior hypogastric plexus block.

Response Testing showed that the interference fields treated in the second treatment had returned. For this reason, a more thorough search was done for any missed fields and a region in between the two halves of large tattoo on the patient's low back was discovered. This new region was injected with 1% procaine. The patient had profound improvement of her low back pain after this treatment, with continuation of no facial pain, and also has begun to experience return of feeling in the previously numb areas of her right pelvic region and thigh that had been affected previously after the lymph node dissection.

CASE REPORT 3

75 year-old male with chief complaint of bilateral foot pain for several years. He reported a long history of running, including marathon running, and that he had been unable to participate in this sport for the last several years because of this foot pain. Surgical history included a compound fracture with open reduction of his left forearm and wrist, and left inguinal hernia repair with mesh placement. Evaluation of his autonomic nervous system by Autonomic Response Testing showed autonomic interference fields at the inguinal hernia and surgical scar, the inferior hypogastric plexus and at all his left wrist scars. The patient elected to do Prolotherapy before doing Neural Therapy. His foot pain improved greatly with the Prolotherapy, however, plateaued at the eighth treatment. Neural Therapy was then done on all interference fields which retested positive, at one week intervals. After six treatments, the patient reported all his foot pain had resolved, and has been able to return to running. His final exam showed no remaining interference fields present. ■

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FOUR-LEGGED PROLOTHERAPY

Canine Hip Dysplasia

Babette Gladstein, VMD

ABSTRACT

Canine Hip Dysplasia (CHD) is a significant health problem among all dogs. It has been estimated that up to 30% of the canine population are effected. As a result, one of the most frequent applications of Prolotherapy involves the hip area. Preventative therapies can play a large part in the management of nonsurgical CHD patients. This article reviews canine hip dysplasia cases treated with Prolotherapy.

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KEYWORDS: ACell, Canine Hip Dysplasia, CHD, Prolotherapy.

INTRODUCTION

Canine Hip Dysplasia (CHD) is a significant health problem among all dogs. It has been estimated by many veterinarians that up to 30% of the canine population are afflicted. As a result, one of the most frequent applications of Prolotherapy and related treatments involves the hip area. Here are some of my most recent cases.

In each one, the Prolotherapy solution comprised equal parts 50% dextrose, 2% lidocaine, vitamin B12 and Heels' traumeel. The injections were usually given at the dorsal and lateral aspect of the hip, in one or both hips. Typically, four injection sites were utilized, in and around the articular capsule surrounding the femoral head.

Treatment protocols (the number of Prolotherapy sessions) were determined by the physical findings, as well as the response to treatments and the cessation of clinical signs. The addition of ACell's MatriStem® was introduced at the end of the traditional Prolotherapy sessions and seemed to accelerate the ultimate progress of the case. This treatment, a natural three-dimensional extracellular matrix (ECM), facilitates healing through several mechanisms. It creates an optimal environment for the body to regenerate site-specific tissue, promoting cell growth and renewal by, amongst other mechanisms, attracting different types of collagens and growth factors. It also enhances healing with anti-bacterial, anti-inflammatory and analgesic properties. Typically, the first session would show some progress. After the second session, more progress would be visible. By the third, the clinical signs were mostly resolved. The fourth session of ACell was the one that proved the most significant: the animal would be as near to normal as possible considering the pathology of the case.

CASE #1: BEJINOS THE TIBETAN SPANIEL

Bejinos is a charming Tibetan spaniel with the breed's regal bearing and energy. Yet upon examination, the nine year-old spaniel was lame and not his cheerful self. Bejinos presented with lameness in his right hind, registering as a 1 out of 5 on the lameness scale. Physical investigation revealed pain and crepitus in the hip area around the femoral head. Other factors, such as tenderness between the femur and tibia at the knee, and laxity of the patella, contributed to his condition. The problem was compounded by the wear and tear on Bejinos' left side. The elbow and shoulder on that side were stiff and sore, problems directly related to overuse.

In his first Prolotherapy session, Bejinos received an 8cc injection of solution. In the same session, his right knee was injected with 4cc of solution at the following sites: the lateral tibial collateral ligament, under the infra patella bursa, into the tendon of the long digital extensor and deeply into the joint space under the patella ligament. A week later, Bejinos underwent an identical second treatment. After this treatment, his lameness issues resolved to a mild stiffness. He was still slightly painful on palpation of the hip area one month later. The owner reported that Bejinos' improvement was promptly apparent. "He plopped down a couple of times in the first week but he hasn't done that for a while." At this third session, Bejinos received 5cc of ACell's in the right hip and knee.

In Bejinos' case, the results were clearly evident, with the compact dog quickly regaining his playfulness and energy. His grateful owner told me "Bejinos is really doing well as far as running around and being peppy. It is wonderful to see. He is spry again. Love it!" His case underscores the value of a combined regimen of Prolotherapy and stem cell injections.

CASE #2: THE SOLUTION FOR SUBI

Subi, the little Shitzu, was clearly uncomfortable at her first visit, with lameness scores of 2 out of 5 coupled with a grade 4 of 5 bilateral patellar luxation. On physical examination, minimal cranial draw on both knees was noted, but mild extension and flexion of her right hip elicited a pain response. Palpation around both coxofemoral joints produced discomfort, as did slight manipulation of the right stifle joint.

X-rays of the 10 year-old, slightly overweight dog showed severe bilateral hip dysplasia with subluxation of the right hip. (*See Figure 1.*) Her previous vet had already prescribed Metacam® and tramadol. Following discussions with her owner, we decided to take her off the medications and begin a regimen of Prolotherapy, omega-3 fatty acids, Adequan® injections, and a course of natural anti-inflammatories. In addition to this program, Subi received a course of three Prolotherapy sessions in each hip using 4cc of the formulation given at three week intervals. Subi's right knee was injected with 2cc of the same solution, at the lateral tibial collateral ligament, under the intrapatella bursa, into the tendon of the long digital extensor, and deeply into the joint space under the patella ligament.

The results of Subi's Prolotherapy treatments and her maintenance program have been gratifyingly pronounced. Although still mildly stiff, Subi soon began to run and play again, exhibiting a near-normal range of motion and functioning. Her owner had not seen this type of behavior from her for at least two years.

Subi was seen for a check up 11 months after her initial visit. She was found to have mild pain and crepitus around the right coxofemoral joint. Her left hip, however, seemed normal. Both patellas were found in place and there no signs of draw on either knee. As maintenance, she received one Prolotherapy treatment followed by a second treatment administration of ACell (5cc), in both hips, two weeks after her Prolotherapy.

Subi, 10 year-old female spay Shitzu, enjoying fall in the park.

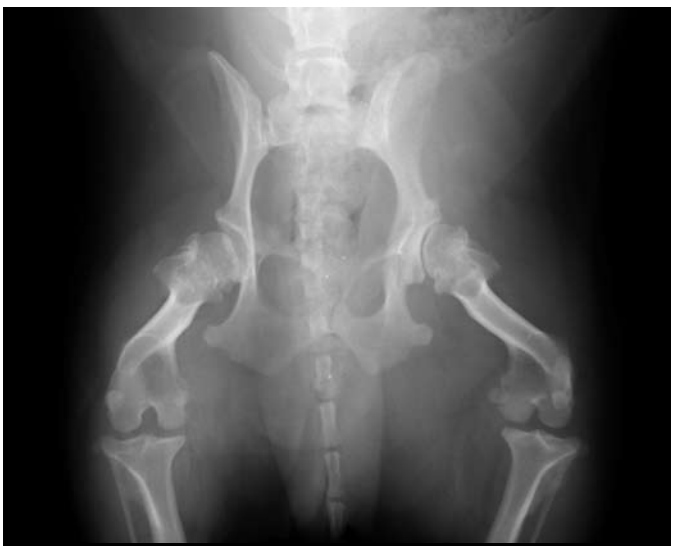

Figure 1. Subi's X-ray shows bilateral shallow acetabulums and a right femeoral head subluxation, with a thickened or remodeled femoral head and neck indicative of degenerative joint disease.

CASE #3: HAZEL'S NEW HOME

Although the young Saint Bernard did not show full signs of hip dysplasia yet, something was definitely going on. She was reluctant to go up or down stairs and would sometimes sit down abruptly in the middle of a walk. Just 2½ years-old, Hazel certainly had bilateral shallow acetabulums (hip sockets) and physical exam indicated that her lower back, as well as the coxofemoral joints of both hips, were moderately painful. (*See Figure 2.*)

Fortunately, since Hazel's new adopted family lived in a Manhattan townhouse with many stairs, the Humane Society opted to treat the condition prophylactically. The chosen course of action involved a Prolotherapy treatment with 10cc of solution. As with the other CHD cases, the treatment was injected at the dorsal and lateral aspect of the hip at four sites in and around the articular capsule surrounding the femoral head. In Hazel's case, like Subi, the treatment was administered to both hips.

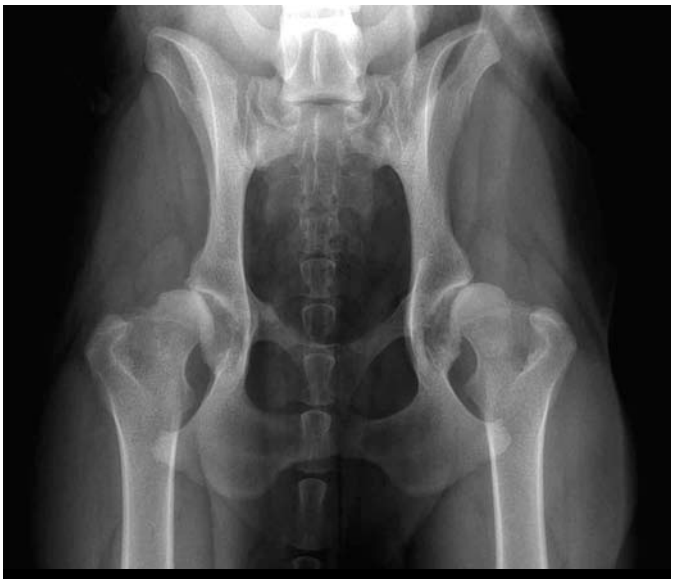

Figure 2. Hazel's X-ray shows bilateral shallow acetabulums and subluxation of the femoral heads. No remodeling of femoral head or neck is visible at this time.

Again, the results were profound. Within a week, Hazel had been more active, sitting down less often, and now being willing to go up or down stairs. There seemed to be less tenderness in the hip joints. A second session was followed up with ACell, 6cc in both hips, two weeks later. Hazel was now ready for her new home. Her owner has scheduled more treatments to maintain Hazel's improved condition.

Hazel, 2 ½ year-old female spay St Bernard, is much happier after Prolotherapy.

CASE #4: THE BUDDY SYSTEM

Several months ago, Buddy, an 11 year-old chow mix at the New York City's Humane Society, presented with hip dysplasia and little hope. Palpation showed how much pain he was in, with touching hind legs and an inability to get up and down comfortably. (*See Figure 3.*) He was basically walking on three legs, and was only using one hind leg for balance.

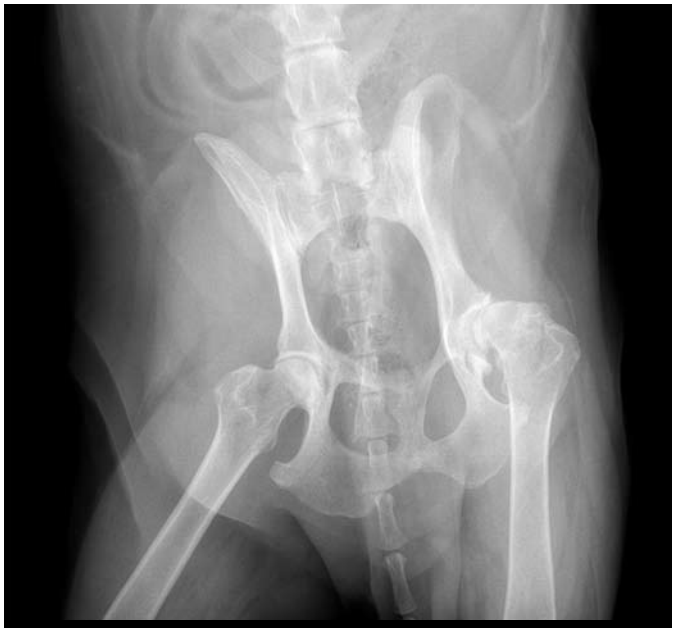

Figure 3. Buddy's X-ray shows a left femoral head and neck with a thickened and remodeled. This is indicative of degenerative joint disease and hip dysplasia.

Buddy's immediate treatment included two Prolotherapy sessions, given at two week intervals and followed by a third treatment of ACell injections. In Buddy's case, Prolotherapy consisted of a 7cc solution. As with the other dogs discussed, Buddy was injected at the dorsal and lateral aspect of the hip, in and around the articular capsule surrounding the femoral head. Both of Buddy's hips were treated.

In the weeks following treatment, Buddy made considerable progress. He was able to get up and down more easily and no longer needed pain medication. He now runs along happily on his daily walks and the closeness of his hind legs has gradually lessened. They now stand about four to five inches apart. He is bearing weight on all four limbs.

A third Prolotherapy session on both hips recently has helped with some residual soreness at the top of the left coxofemoral joint. But the success of his Prolotherapy treatment is not the only good news for Buddy. He has recently been adopted and is going to a new home along with his long time companion, a yellow lab mix.

Buddy, 10 year-old male neuter, happy to be running and playing.

CASE #5: OUT OF THE SHADOW OF PAIN

When I first saw him, Shadow was suffering badly with dysplasia, as you can see in *Figure 4*. Stairs were out of the question for this 10 year-old German shepherd mix and his owner, upset by Shadow's deteriorating mobility, built a 100 ft ramp behind her Brooklyn brownstone so that the much-loved dog could get out to the yard.

My recommendation was to treat Shadow over three Prolotherapy sessions, administered at two week intervals. At each session, he received a 7cc injection in each hip area. Shadow's fourth session included a treatment of ACell. The very first treatment required that Shadow be anesthetized and this was done with .7cc of Telazol®. Shadow was also placed on weekly Adequan® shots to help him with his arthritis.

Here's what Shadow's owner has to say about the transformation she's seen in her dog: "In the period of a month and a half, you cannot believe the difference in his walking and how he is able to go up and down stairs and he is in a lot less pain."

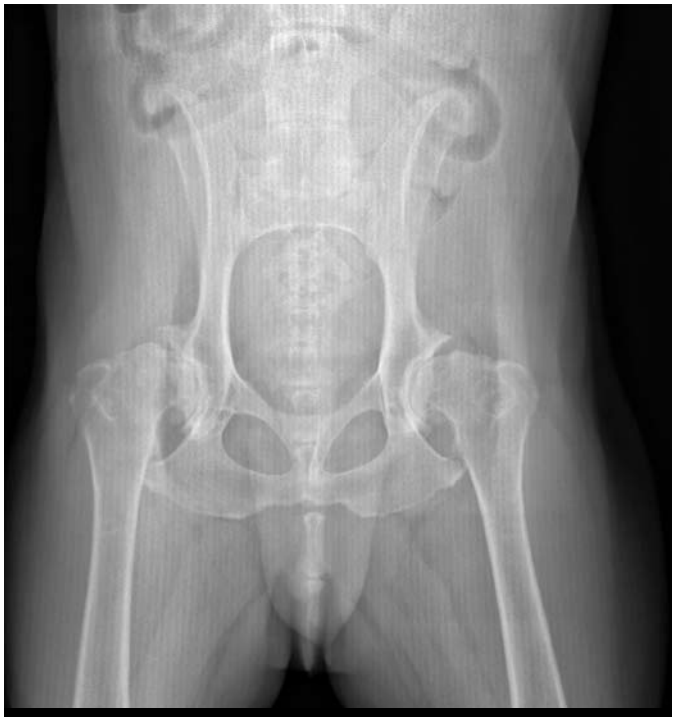

Figure 4. Shadow's X-ray shows bilateral shallow acetabulums with a thickened or remodeled femoral heads and necks, more severe on the right hip. This is indicative of degenerative joint disease and the cause of his lameness.

Shadow, 10 year-old male alter German Shepard mix, in his park yard.

CONCLUSION

Preventative therapies can play a large part in the management of nonsurgical CHD patients. By creating the greatest possible musculoskeletal support and keeping the hips pain-free, good range and function are maintained. This support can delay or possibly prevent degenerative joint disease. Therefore, CHD patients benefit from early detection and treatment with Prolotherapy. ■

TEACHING TECHNIQUES

Alternative Positioning for Injecting the Iliolumbar and Short and Long Dorso-Sacroiliac Ligaments using Prolotherapy

Ann Auburn, DO, Scott Benjamin, PT, DScPT, Roy Bechtel, PT, PhD

ABSTRACT

Background Content: *This skill paper investigates the ramifications of an alternative method to inject the iliolumbar (IL) and the dorso-sacroiliac ligaments (DL). Both the IL and the DL are very important to pelvic control and are needed for sacral stability. The IL and the DL are needed during functional and exercise activities but with the ligaments being injected only in the prone position they are not being supported in a variety of torsional positions.*

Purpose: *The purpose of this skills section is to look at injecting the IL and the DL in a prone functional exercise position and also in a static standing position to provide both ligaments with the means to be injected during physical therapy exercise activities and during a torsional hip position.*

Study Design: *Single case study.*

Methods: *One subject, a 45 year-old male participated in this skill section. The participant used an exercise ball and went into the exercise position to strengthening the lumbar multifidus muscle. During that position, the iliolumbar ligament and the dorso-sacroiliac ligament was injected to provide stability to the pelvis during this physical therapy activity. The second position showed the participant standing with his right hip flexed in a posterior direction (as in walking up stair, an incline or during sitting) and then the IL ligament was again injected.*

Conclusion: *Since physical therapy can put undue stress upon the pelvis during exercises and rehabilitation, this injection method may provide a benefit for patients who experience lower back pain. The lumbar multifidus is a focal point in physical therapy rehabilitation. With strong ligament support for the lumbar spine and pelvis, the outcome for rehabilitation can become even more beneficial. The positioning will provide the treating physician with an alternative to conservative injections methods and give the ligaments in the pelvis the opportunity become even stronger.*

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KEYWORDS: dorso-sacroiliac ligament, Iliolumbar ligament, multifidus, Prolotherapy.

The spine is a flexible biomechanical system that will support motion from a variety of positions and contortions. The ability to do this is brought about by a vast array of intricate interwoven connections that include ligaments, joint capsules, discs, muscles and the nervous system. It has been demonstrated that in Western society, low back pain (LBP) is among the most costly ailments to treat and one of the most common reasons for patients to seek health care.[1] Frymoyer et al [2] reported that the prevalence of the LBP was between 60 and 80% in the United States, which had a larger percentage of LBP cases than European countries.[3] In the vast archives of the physical therapy literature, there has been much discussion regarding the importance of the lumbar multifidus muscle and its role in preventing recurrence, for patients with LBP.[4-8] Evidence suggests that muscles are the body's first line of defense against externally-applied forces.[4, 9] A fully functioning neuromuscular system is the best guarantee of continued spine health.

ANATOMY AND FUNCTION

In order to see the importance of muscles to enable normal spine function, we need to discuss the anatomy of the multifidus muscle. The multifidus is one of the most medial and deepest portions of the low back muscles. The muscle is innervated by the medial branch of the dorsal ramus of the spinal nerve at each vertebral segment.[1, 2, 4] Multifidus is usually divided into superficial and deep portions. The deeper portion spans one vertebral segment, while the more superficial portion spans several segments. The deeper portion is composed mainly of type one (slow fatigable) fibers, while the superficial portion is composed mainly of type two (fast fatigable) fibers.[4] The multifidus is generally regarded as an extensor and side flexor of the spine. However, little regard has previously been given to its stabilizing function, a task which falls mainly to the deeper fibers.[2, 4] But, what happens if there is a disruption to the multifidus due to injury and/or surgery and the bone to bone (ligamentous) system begins to experience increased demands for its stabilizing contribution? When this occurs, a person may have disruption in their spine segmental stability and this can lead to poorly-controlled segmental motion, sacroiliac dysfunction and decreased ability for a person to meet the demands of normal function. The ligamentous structures that we need to focus on are in the pelvis and lumbar spine.

FOCUSED LIGAMENTOUS STRUCTURES

For our purposes, the major ligaments that we will focus on are the iliolumbar (IL) and the short and long posterior dorso-sacroiliac ligaments (DL). (*See Figure 1.*) Both of these ligaments will resist the bone to bone movement during daily activities. For example, the IL will resist motion at the L4-L5, L5-S1 segmental level as well as will resist ilium motion on the L5 segmental level. The DL will resist sacral motion in a posterior direction and this will aid stability of the S-I joint.[10, 11] The joints are supported by these ligaments and if the muscles are not strong enough, motions can become restricted and painful. Since the ligaments of the pelvis and lumbar spine have to resist motion during an array of activities in daily life including work and recreation, we want to discover a way to enhance the stability of these structures.

PROLOTHERAPY RATIONALE

Prolotherapy has been discussed and used from the 1960s forward.[12, 13] Much knowledge has evolved as regards the usage of a variety of natural medications, and also the structures that have been targeted.[14] Prolotherapy is most appropriate for patients who have CLBP and pelvic instability, ligamentous laxity. The literature supports the use of proliferation therapy for patients with LBP and also with knee injuries, ankle instability, lateral epicondylitis and even plantar fasciitis.[15-19] The traditional way to inject the IL or the DL is to have the patient prone[15-19] with a pillow under their trunk. Auburn et al, (2009) have shown an alternative functional method of injecting these ligaments by changing the angles at which the ligament will be stressed when an injection is applied. This technique was performed in a semi-standing position. We have taken the functional method one step further by having the patient (author two) move into the strengthening positions for the multifidus muscle and then applying an injection to the IL and the DL ligaments.

Traditionally, the multifidus is strengthened in the prone position, but we have increased its recruitment by leaning over a ball and having the patient work in variety of patterns. (*See Figure 2.*) Bechtel, et al [20] have shown that via rehabilitative ultrasound (RUS) the multifidus is more efficiently recruited in the quadruped position than in the prone position. RUS has been shown to be an effective tool to view muscular and ligamentous structures.[21] Since the ligaments play such a significant role in the segmental stability during strengthening work, we wanted to have

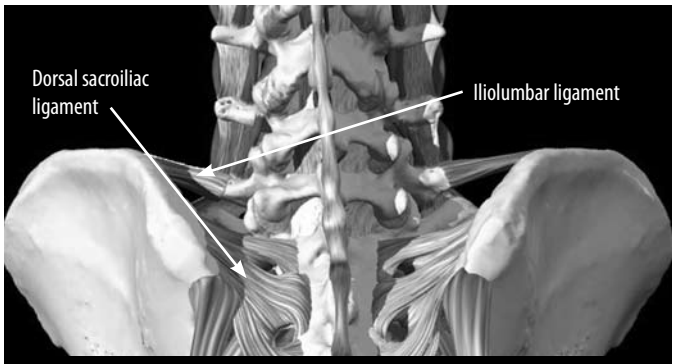

Figure 1. Illustration showing the left iliolumbar and the left dorsal sacroiliac ligaments as noted by the arrows. Courtesy of Primal Pictures, 2003.

Figure 2. Illustration showing the starting position for multifidus strengthening and iliolumbar and dorsal sacroiliac ligament injections.

the patient work the muscle but also support the spine; thus we injected the IL and the DL during the particular strengthening activity. Quadruped position exposes the highly stressed areas of the ligament. By having the patient contract the muscle, stress on the ligamentous system is reduced thus reducing pain and giving the Prolotherapy a better opportunity to work. Being that we had the patient get into the exercise position and still used the rule that we would inject at the insertion of the ligamentous structure, this would not obviate the chances of the material getting into the ligamentous structure. We had the patient abduct their leg, putting more pressure on the multifidus, but also needing more stability from the ligaments to hold the position. (*See Figure 3.*) Therefore, by gaining muscular control in this position, we can increase the segmental stability, decrease strain on the ligaments and hopefully improve the effectiveness of the Prolotherapy injections.

ALTERNATIVE STANDING POSITION

The alternative standing position was for injection of the iliolumbar ligament (IL). Our thought here is to put the one side of the pelvis in a position where it would expose the most-stressed portion of the IL prior to injecting it.

Figure 3. Illustration showing the starting position with the leg abducted for multifidus strengthening and injections of the iliolumbar ligament as shown with primary author (AA).

(*See Figure 4.*) Why? Because if you take your right leg, as shown in the illustration, and move it where the knee and hip are bent into flexion, you will cause posterior rotation of the right ilium. When that occurs, you will stress the IL ligament and by injecting this ligament in such a manner you can achieve maximum effectiveness of the injections and keep the ilium stable during activities such as going up stairs, move from a sitting to a standing position and also when you are running. We believe that these new procedures should ultimately help patients to achieve the goals of smooth systematic fluid motion and pain-free function faster than traditional methods. ■

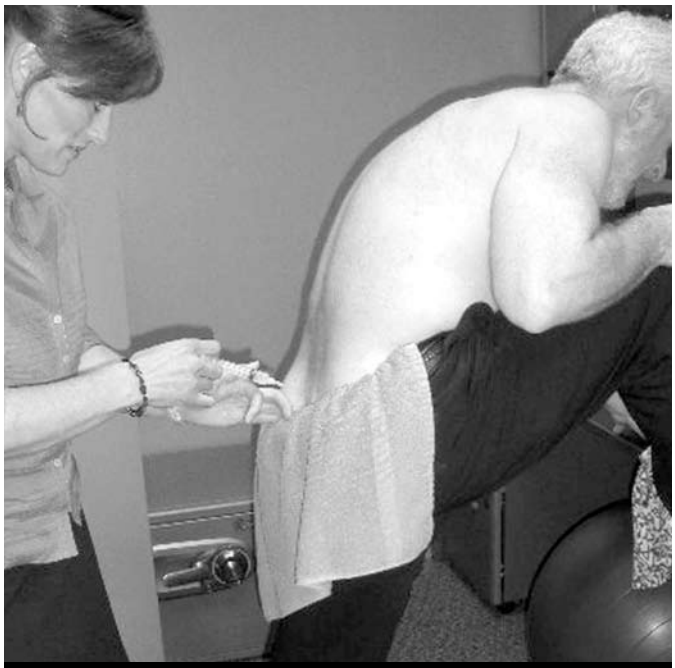

Figure 4. Illustration shows the alternative injection method for the iliolumbar ligament or the long or short dorsal sacroiliac ligaments with Dr. Auburn injecting the Prolotherapy solution.

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TEACHING TECHNIQUES

Prolotherapy Tips for Beginners: How I Started with Prolotherapy

Gunter Baehnisch, MD

I wish to help make hospital and practice-based colleagues aware of Prolotherapy. So, I will tell you how I started with Prolotherapy. After completing my study of medicine at the University of Leipzig, in 1972, I worked at the orthopedic clinics at the Universities of Leipzig and Würzburg, Germany. Then, after finishing my clinical education, I switched to musculoskeletal medicine and manual therapy. I received specialized training in the Cyriax technique for orthopedic medicine.

I had opened a private practice in downtown Leipzig in 1994. At that time, Dr. Funck, in Lübeck, was already successfully applying Prolotherapy in treating causes of spinal and joint pains, and gave me my initial instruction. Thereafter, I took several courses with Dr. Tom Ravin in Denver, Colorado, and I bought the basic work on Prolotherapy *Ligament and Tendon Relaxation treated by Prolotherapy* by G.S. Hackett, MD.

After returning home, however, I did not immediately start applying the new procedure. One of the reasons was the fact that we did not immediately change our everyday routines with methods of treatment that had been handed down for years. But the main reason for my initial reticence was just the normal nervousness of a beginner.

This changed, however, when a 53 year-old patient turned up who complained of one-sided hip pains, especially when climbing stairs or when getting up from a seated position. To specify the area of pain, she put the fingers of her right hand on the large trochanter. She reported that she had gone through a whole series of unsuccessful specialized consultations. She vividly explained that imaging methods such as X-rays, nuclear spin tomography and bone scans did not result in any clinically relevant findings. Above all, there were no signs of wear and tear to be found in the hip region. A clinical function test did not result in any relevant negative findings either.

The patient also reported that she had rather intense pain when turning over in bed or when lying on the hip where the pain was located. She did not get better, in spite of extensive therapy, including physical applications, chiropractic and acupuncture. Therapists were at a loss with such relatively long-lasting symptoms.

What made the greatest impression on me in the case of this patient was the considerable pain that I provoked when pressing on the region with my thumb.

When examining the patient I used the following procedure:

1. I put one hand around the region of the trochanter major mandibulofacially and pressed the region with the thumb of my other hand. (*See Figure 1.*) Then I asked

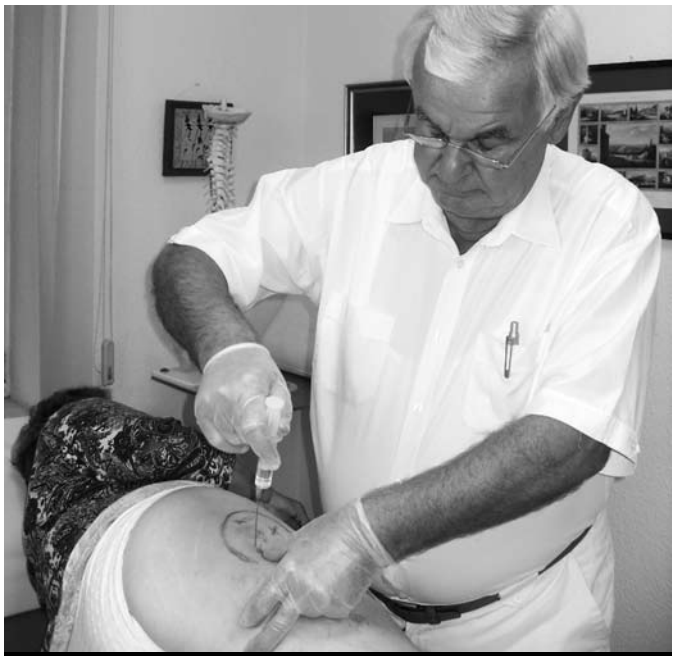

Figure 1. Dr. Baehnisch demonstrating Prolotherapy to the greater trochanter.

the patient how intense the pain was to enable myself to clearly identify the pain areas on the large trochanter. I carried out a side-comparison examination to enable the patient to compare. The pain areas identified were marked in dots with a marker.

Immediately after marking the pain areas, I explained the causes of the pain to the patient in detail as a consequence of the instability at the base of the tendon at the large trochanter. The next step was to explain the procedure of the treatment to her and propose using the pepper technique to infiltrate the pain areas that are in contact with the bone with 20% glucose solution.* I explained to the patient that the glucose solution used in Prolotherapy enhances collagen synthesis. Finally, I informed the patient that normally three sessions at intervals of two weeks are needed.

2. Explaining the gradually continuing cascade-shaped reconstruction processes in the area of the base of the tendon that reduce the symptoms was particularly important to make sure that the patient understood the situation. No less important was explaining that this was a developmental process for reducing symptoms. In other words, it was not just simply a question of getting an injection and making the pain go away. Since this patient had substantial pain over a longer period of time and had gone through a whole series of unsuccessful specialized consultations (mostly with surgeons, orthopedic surgeons and neurologists) with the corresponding apparatus diagnostics, she consented to the therapeutic procedure. She was also sufficiently patient in her expectations of a reduction in pain during the treatment.

There were three injection sessions, over a period of three to four weeks. After the third session of therapy I agreed to another appointment for a check-up after three months. As it turned out, this relatively long time between appointments proved to be beneficial because this was the period of time when there was a significant reduction in pain. I recommended the patient to live normally, subject herself to normal stress and strain, and I appealed to her to be patient in her expectations of a reduction in pain.

We quickly had our first "sensational success." The patient reported that she had fewer symptoms, and none at all about three months after the last session. She also reported that she was able to stand, walk and climb stairs normally without any impairments, and even was able to lie on the hip that had previously caused her pain.

The initial experience I had with Prolotherapy led to localizing other areas of the locomotor system and supporting apparatus in continuing to expand our range of treatments. For instance, over the years, I have seen that Prolotherapy treatment is very efficient and promising for treating pain caused by connective tissue damage syndrome.

I recommend that anybody who intends to learn the principles of Prolotherapy, and introduce them to their own practice, follow this procedure:

1. Start off by reading the basic work on Prolotherapy: *Ligament and Tendon Relaxation treated by Prolotherapy*, by George Stewart Hackett, MD, Gustav A. Hemwall, MD, and Gerald A. Montgomery, MD.

2. Attend courses on the topic of Prolotherapy established and conducted by experts.**

3. Start with Prolotherapy in your practice immediately after completing the training courses. If you should still be reticent, I recommend overcoming your reticence by first treating your patients who complain of pains caused by instability at the large trochanter. If you, as the person treating, and the patient being treated can muster the needed patience and composure, you will inevitably be rewarded with successes in your first Prolotherapy. Indeed, you will not be able to avoid extending your range of treatments as you learned it from your initial study of the literature and attending courses. ■

EDITORS NOTES

* Additional illustrations detailing Prolotherapy to the hip can be found in the *Teaching Technique* column in *JOP* Volume 1, Issue 2.

** Please see the *Skill Enhancement* section for more information on upcoming seminars and organizations.

IT'S A WIDE WIDE WORLD

Literature Review: Popliteal (Baker's) Cysts of the Knee

Gary B. Clark, MD, MPA

BEFORE PROLOTHERAPY...THERE WAS SCLEROTHERAPY

Case Study: *A 52-year-old white male initially presented with an acute, complex tear of the posterior horn of the medial meniscus, confirmed by MRI. Physical therapy and nonsteroidal anti-inflammatory drug (NSAID) treatment suppressed neither his pain nor disability. Then, over the next 2 years, a posterior right knee popliteal swelling developed. MRI imaging proved this swelling to be a Baker's cyst extending into the upper gastrocnemius muscle. The patient continued to experience posterior knee pain with decreased range of motion. (cf. Centeno)*

INTRODUCTION

Regenerative Prolotherapy is useful for treating soft tissue injuries other than the classic joint sprain injuries. In this light, Prolotherapy has been practiced under the name of "*Sclerotherapy*" (and variations of that theme) since the days of Hippocrates—that is two millennia! As such, Sclerotherapy has become a time-honored treatment and a cure for many developmental and acquired soft tissue lesions—including soft tissue cysts.

POPLITEAL KNEE CYSTS

Along with the vast multitude of maladies that beset the human condition, there are benign, soft tissue cysts. These include a huge number of different kinds of developmental and acquired cysts of virtually every tissue of the body. Amongst those are the popliteal or, so-called, Baker's cysts of the knee—which are "not infrequently" encountered in musculoskeletal or orthopedic medicine.

Occurring in the hollow behind the knee (i.e., the popliteal space), Adams generically described these popliteal cysts in 1840.[1] Baker more clearly delineated these cysts in 1877 as "synovial cysts in the leg in connection with disease of the knee joint" and which, he reported, were often associated with the bursa of the semimembranosus tendon.[2] Now, these popliteal cysts are named after that same Dr. William Morrant Baker.

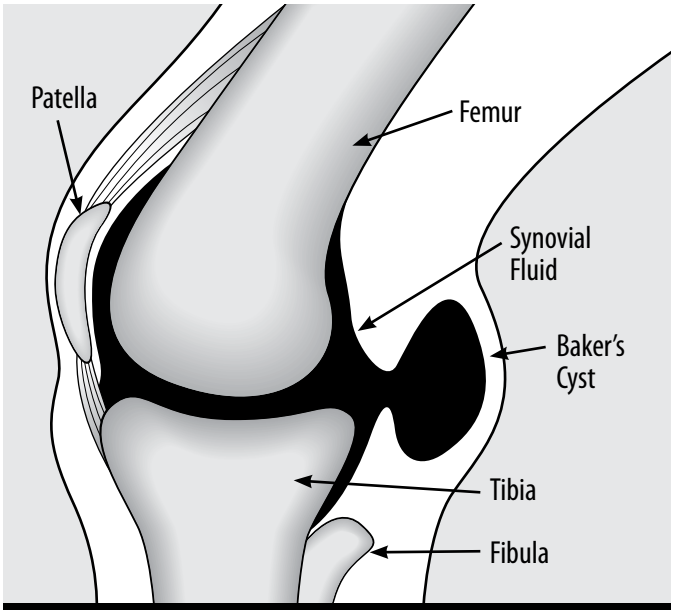

Illustration of a Baker's cyst.

Morphology: In adults, a Baker's cyst characteristically involves a protrusion of the knee joint space lining (i.e., synovium) producing a posterior bulging into the popliteal space behind the knee. This popliteal cyst usually arises between the tendons of the medial head of the gastrocnemius and semimembranosus muscles, posterior to the medial femoral condyle. It often extends (dissects) into one or the other tendon, more often that of the semimembranosus.

For years the earliest clinical literature associated the popliteal cyst with involvement of the semimembranosus tendon and bursa. With the advent of more sophisticated imaging techniques, however, these cysts more

characteristically reported in association with posterior meniscal tearing—often accompanied by knee arthritis and/or loss of articular cartilage. The fluid-filled cyst almost always maintains an open communication with the knee joint space via the meniscal tear. On occasion, the joint-space/cyst-space communication may become obliterated by spontaneous articular tissue healing. In any case, the space-occupying cyst ultimately becomes a swollen mass lesion in the popliteal space, reducing knee range of motion, creating stiffness and pain, and impinging on nearby vital structures.

The advent of MRI and ultrasound imaging has greatly aided our understanding of the overall pathology. There is a reported 5-18% general prevalence rate by MRI and a 40-42% prevalence rate by ultrasound. Eighty-three percent have been associated with meniscal tears—most frequently involving the posterior horn of the medical meniscus. Thirty-two percent of the meniscal tears have been associated with anterior cruciate ligament tears with subsequent joint instability. Forty-three percent have been associated with articular cartilage damage.[3, 4] In contradistinction, meniscal cysts, which are morphologically related, are characteristically smaller, occur along the periarticular margins of the menisci, and are almost always associated with horizontal meniscal tears—the lateral meniscal edge being a more predominant site than the medial.[5]

Popliteal cysts also occur in the pediatric age group. However, no predominant underlying joint abnormality has been reported with cysts of this age group. They appear to be more developmental in nature and only rarely communicate with the articular joint space. Baker's cysts in children almost always disappear in time, seldom requiring interventional treatment.[6]

Natural Complications: The pressure of the swollen popliteal cyst may compress and partially occlude the popliteal vein causing secondary, lower leg edema and true deep vein thrombosis (DVT). Occasionally, the cyst may actually rupture, producing acute popliteal and lower leg pain, swelling, and redness—adding to the challenge of the differential diagnosis.

Differential Diagnosis: First and foremost, an accurate diagnosis is obtained through a complete history and physical examination. The major differential diagnoses of a popliteal mass include:

1. Deep vein thrombosis (DVT) with thrombophlebitis (i.e., especially differentiating DVT from the calf pain, swelling, and redness of an acutely ruptured popliteal cyst).
2. Popliteal artery aneurysm.

Ultrasound and MRI are extremely useful in confirming the differential diagnosis and verifying cyst communication with the joint space. Overall, ultrasound may be more efficacious (effective and cost-efficient) than MRI—certainly less expensive.[7]

Treatment: If they are not symptomatic—Baker's cysts do not require any treatment. If symptomatic, they have been treated with the following approaches:

- Just leg rest, ice, and elevation may suffice. Instead of ice, a heating pad may help some individuals. Avoiding squatting, kneeling, heavy lifting, climbing, running, and any other activity that puts strain on the posterior knee may be helpful. Specific physical therapy and other body work (e.g., Rolfing, Pilates) may be helpful in stretching the hamstring muscles and conditioning the quadriceps and its tendons.
- Ace bandage compression and bracing of an unstable knee may be helpful. An actual knee brace, however, can further compress the already tender popliteal space.
- NSAID medication has been reported as fleetingly helpful if there is any substantial inflammatory component.
- Cyst aspiration (drainage) may be curative.
- Cyst drainage and injection of corticosteroid into the cyst space have been reported, again, as helpful if there is an inflammatory component—still, albeit, only fleetingly.
- The Mayo Clinic reports using Prolotherapy since 2005 and finding it curative.[8]
- Surgical excision is mentioned but should be held in reserve for only the most extraordinary of cases.

Our main intention is to familiarize both Physician and Patient with the history, basic concepts, and language of Prolotherapy—as well as whatever literature exists that provides a base of evidence confirming its clinical efficacy. With this article, we would like to stimulate reading and increase the general level of understanding

of Prolotherapy (or Sclerotherapy) of Baker's cysts—as well as to stimulate interest in improving private clinical and academic research evidence of the efficacy of such treatment. Please use Google and the website for the National Library of Medicine (www.pubmed.gov) to access the following and other articles on the internet. Thanks to the publisher, the following article is readily available in its entirety by searching for it by author and subject via Google.

TREATMENT OF BAKER'S CYST

Sclerotherapy of Baker's cyst with imaging confirmation of resolution. Centeno CJ, et al. *Pain Physician*. 2008 Mar-Apr;11(2):257-61.

ABSTRACT SUMMARY

Centeno, et. al. (2008), presented an "isolated case report" of treating a 52-year-old male patient for Baker's cyst—the patient's general history being classic, as previously described. The main objective of this single-case management report was to observe whether the already recognized curative effect of Sclerotherapy on a Baker's cyst could be verified by MRI imaging changes.

Initial conservative treatment of the patient's right popliteal cyst consisted of NSAID medication; drainage of the swelling, once a month, for three months; along with physical therapy. Each drainage was performed posteriorly and produced about 40cc of clear serous fluid, causing 1-2 weeks of symptomatic relief of pain and stiffness. Then the swelling, pain, and disability would resume.

Because of persistent recurrence of the cyst and its symptoms, the authors began three monthly combined treatment sessions, consisting of complete drainage and proliferant-sclerosant injections.

- After draining the Baker's cyst from the posterior aspect of the knee, the authors injected 3 to 5cc of their proliferant solution into the joint space. This solution consisted of approximately 15% dextrose, 10% sodium morrhuate, diluted in .6% lidocaine (*JOP* discussant's estimations). The solution was injected into the joint space anteriorly, i.e., "intraarticular through the medial infrapatellar approach." (sic)
- According to a telephone conversation with the author, sodium morrhuate diluted in lidocaine was also injected directly into the cyst, posteriorly, following each drainage—although this is not clearly delineated in the article.[9]

Within four months of initiating this combined treatment, the patient reported decreased cystic swelling, pain, and range of motion disability—albeit he continued to experience medial knee pain attributed to residual meniscal injury.

Of key importance to the main objective of management of this patient, pre-treatment and follow-up MRI studies were obtained. The 12-month post-injection MRI study revealed complete resolution of the cyst. Thus, the authors suggested there being a positive value of MRI as a follow-up of treatment of Baker's cyst Sclerotherapy. Wisely, they recommended more large scale, prospective case studies to confirm their isolated observation. (Study design: Uncontrolled, single-case report: Minimal level 4 evidence)

JOP COMMENTARY

This article definitely presents descriptive MRI evidence, including radiophotographs, showing cyst resolution following treatment. Perhaps a source of confusion, however, is the interspersion of the two terms, "Sclerotherapy" and "Prolotherapy." The term "Sclerotherapy" is in the leading title. Then, "Prolotherapy" is used seven times and "Sclerotherapy" or "sclerosing" are used a total of eight times. "Prolotherapy" is used in the abstract conclusions and the major heading, "Utilization of Prolotherapy Agent." Then, "Sclerotherapy" appears in the main article conclusion.

It is still arguable between the two camps of Prolotherapists and Sclerotherapists as how the healing of the subject patient's popliteal cyst might be explained.

- Prolotherapists might look at the glass as half-full and say that the healing occurred subsequent to the sodium morrhuate's causing an inflammatory reaction that congregated growth factors, which stimulated fibroblasts to lay down new collagen, "regenerating" a unified fibrous closure, thus, eliminating the cystic space—ergo, a "healing" cascade reminiscent of a "House that Jack Built."
- Sclerotherapists might look at the glass as half-empty and say that the scarring occurred subsequent to the

sodium morrhuate's causing an inflammatory reaction that stimulated fibroblasts to lay down new collagen, creating a fibrous scar, adhering the cyst walls, thus, closing down the cystic space—ergo, a "scarring" phenomenon reminiscent of the scarring of a skin wound.

In the end, it all amounts to being the same healing process—the details of the explanation just depending on how you hold your tongue in your mouth when you say it. The real explanation is that there needs to be a randomized, double blind study to demonstrate the microscopic cellular healing process and confirm the degree of efficacy.

As interesting as the original article is, the two "Letters to the Editor" accompanying the article are arresting, as well. In the first letter, Felix Linetsky, MD, richly complements the Centeno article with a very informative short history of Sclerotherapy, leading to the development of Prolotherapy. He describes the transition of early Sclerotherapy of soft tissue lesions, such as hernias and cysts, leading to the more classic applications of modern-day, musculoskeletal Prolotherapy. His listing of historical references to Sclerotherapy is of definite historical value.

Also, Dr. Linetsky extends this Centeno, single-patient experience by adding a thought-provoking suggestion as to how "Sclerotherapy" might be useful in treating the cysts often found anteriorly to painful zygapophyseal, facet joints of the sprain-injured cervical spine by performing intra-articular facet injections.

In the second letter, Doctors Pinnamaneni and Thomas of SUNY Upstate Medical University provide some interesting historical facts about the earliest reports of Baker's cysts along with citing some information on certain theories of the biomechanical derivation of such cysts. Also, they comment on how important it is that proper MRI imaging of a Baker's cyst should reveal the cyst's communication with the knee joint. In their response, Centeno, et. al., demonstrate that they had, indeed, confirmed MRI study evidence of joint-cyst communication.

Finally, the SUNY correspondents go on to raise skepticism that "Prolotherapy" (not mentioning "Sclerotherapy") could really be the direct cause of the cyst's disappearance. Unfortunately, it seems that these investigative clinicians failed to grasp the difference between "Sclerotherapy" versus "Prolotherapy" as the two techniques were employed in the management of this single-case—possibly due to the way the management plan was reported by Centeno, et. al., in this relatively abbreviated article.

Familiarly, the SUNY correspondents bemoan a dearth of supportive scientific evidence and they pointed out the weakness of a single-case study—summarily dismissing the suggested use of Sclerotherapy/Prolotherapy as treatment of Baker's cyst. They object on the grounds that there is a lack of adequate published evidence of efficacy of Prolotherapy—without paying heed to the literature already extant. In follow-up, Dr. Centeno disagrees with the correspondents regarding their dismissal, pointing out his article's clearly being a single case study, recommending further follow-up scientific study. To repeat a line that Centeno quotes in his own written response:

"Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough."[10] ■

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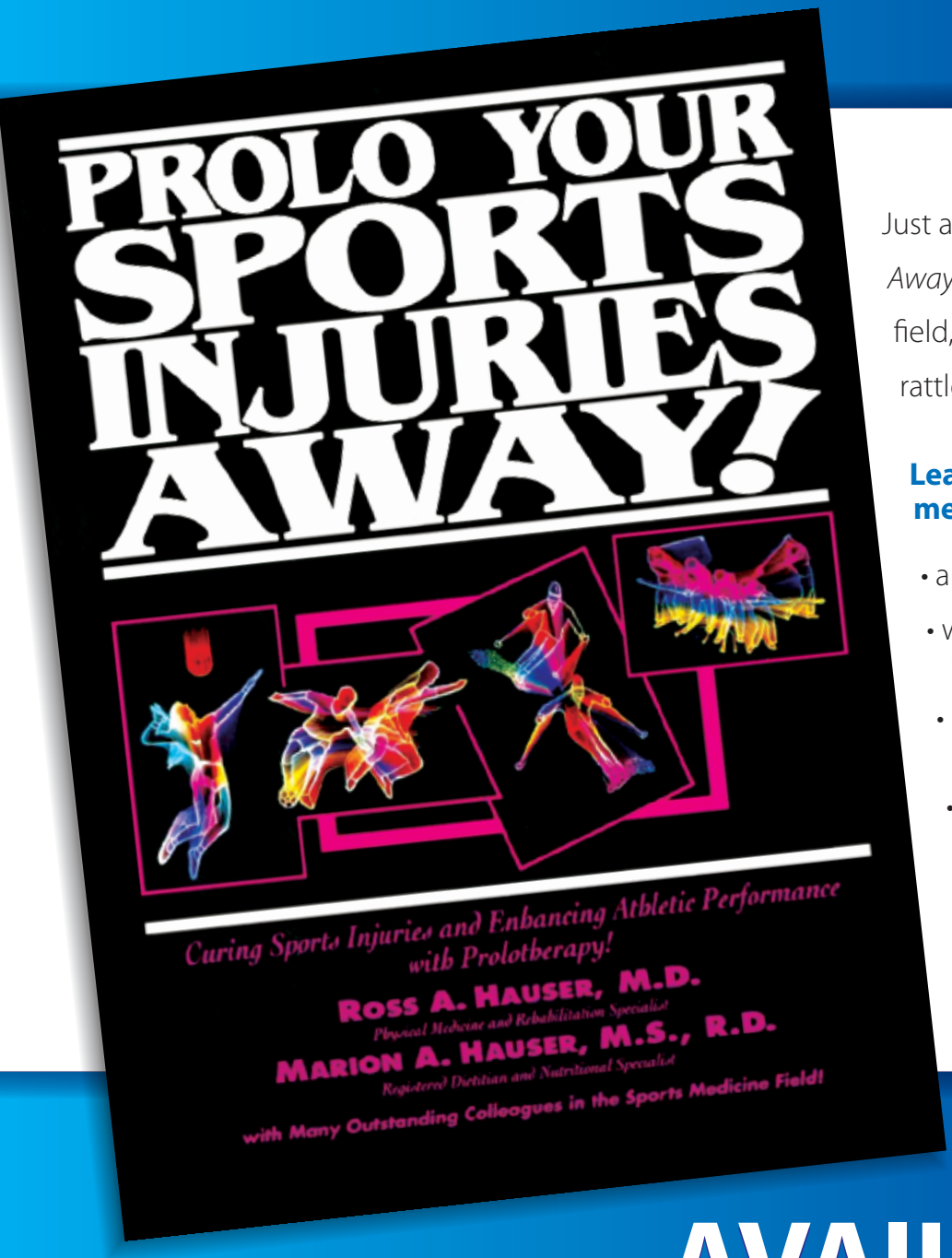

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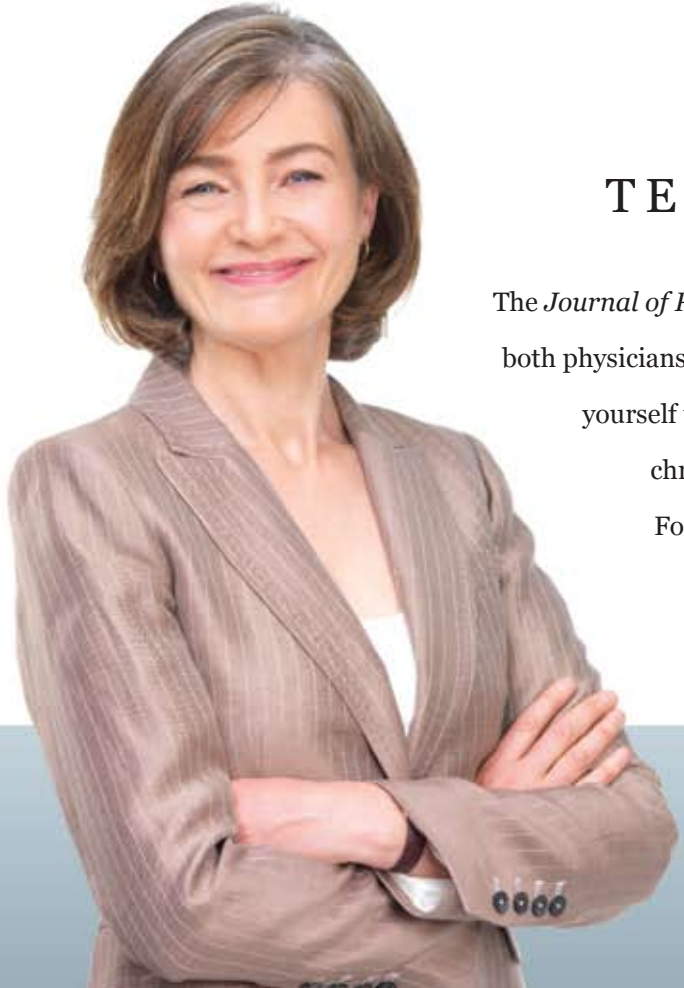

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