

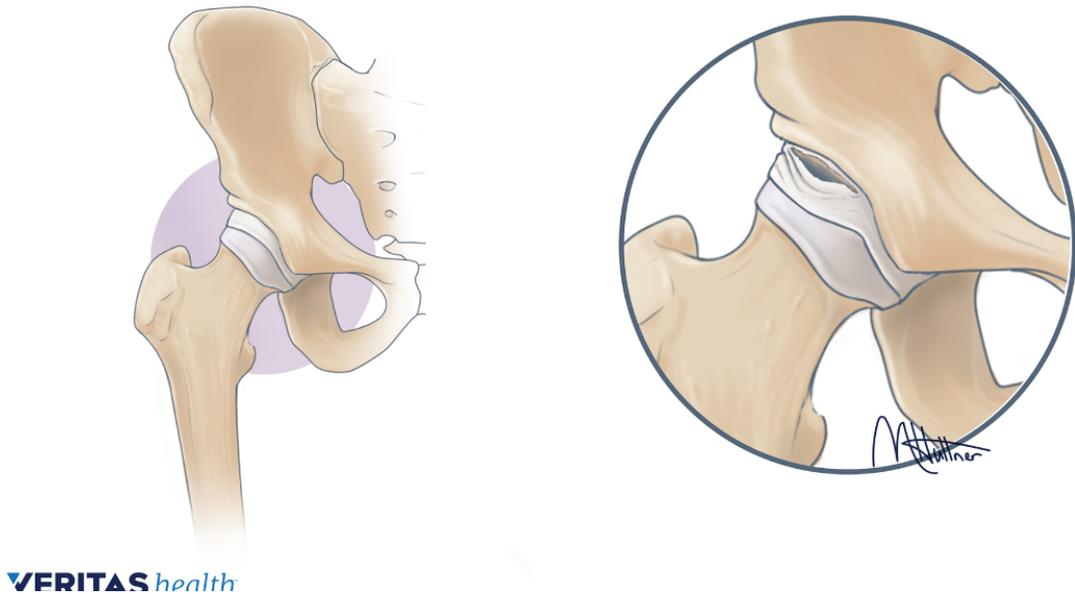
Prolotherapy: Regenerative Medicine and the  
Need for FDA Approval

Senior Thesis  
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## **My Story**

When I was around ten years old I fell off one of my horses and tore the labrum, a ligament, in my right hip. This also knocked my pelvis out of place and it repositioned itself to be able to function like a normal hip. Around the time I turned thirteen years old, I started experiencing severe sciatic pain that no doctor, chiropractor, or physical therapist could explain or treat. I had X-rays and an MRI scan to look at my nerves and bones to see if there was a problem that could have been causing this pain. I then went to a physical therapist who recognized my problem and recommended that I go see Dr. Hauser to have prolotherapy, a procedure that is still considered “experimental” and is not FDA approved, performed. Until I was able to fly to Florida, I saw that physical therapist weekly and had my hip repositioned every time I went. Towards the end of my visits with him for my back, we realized that I could sneeze and my pelvis would pop back out of place and that we were only treating the symptoms but not helping the problem itself.

My mother took me to Fort Myers, Florida where I saw Dr. Hauser and had my initial consultation on my lower back, hip, and pelvis. It was then that I was diagnosed with a torn labrum in my hip, a pelvic symphysis stretched from 5 millimeters to 11 millimeters, and joint hypermobility syndrome. Dr. Hauser decided that I would benefit from Prolotherapy and PRP prolotherapy. I had the procedure done and after only one treatment I could feel a difference in the way I walked, stood, and sat. I went back to my physical therapist to have him check my pelvis after two weeks and I was told that my pelvis was “straight as an arrow.” I had three more treatments done and was finally able to sit for more than 10 minutes without having to shake my right leg to distract myself from pain.



For most of my junior year and the first few months of my senior year of high school, I suffered from debilitating migraine headaches that rendered me incapacitated for days at a time. I missed days of school and got behind in many of my classes. I started going back to my physical therapist to have the knots in my shoulder muscles relieved. He then told me that I would need to go back to Florida because, again, we were only treating the symptoms. We finally went back down to Florida and I had my consult for my neck. I was then diagnosed with severe cervical instability, meaning that the ligaments in my neck were severely loose, causing my muscles to have to pick up their slack, making my muscles excessively tense. The muscle tension in my shoulders and head led to tension headaches that caused pain from my shoulder muscle, through my occipitofrontalis muscle, the muscle that runs from the back of the head to the forehead, to my eyebrows. I had a digital motion x-ray (DMX) scan done to show my cervical instability and to show Dr. Hauser which parts of my neck were the least stable. I was treated five times and

after one treatment I, again, saw immediate results. The treatments did cause me to have immense headaches anywhere from 24 to 72 hours after treatment, but the headaches became less and less intense.



While I was having my neck treated, I noticed that my sciatic pain, pain that ran from my pelvis down the back of my leg through the sciatic nerve, was coming back and I was having new pain in my right knee. After having my pelvis treated, we were told that oftentimes patients do have to return for a “booster” treatment a few years down the road to ensure stability. I had an extra treatment on my lower back and a new treatment on my knee and, while they were the most painful treatments that I can remember, I have not experienced sciatic pain and my knee pain has decreased substantially. After my second treatment of my right knee and “booster” treatment of

my low back, I was in a lot of pain but I could tell that my ligaments were tighter and there was a difference in how my legs moved when I walked.

### **The Need for FDA Approval**

I am extremely fortunate to have parents who support me and want me to be comfortable at any cost. My parents were able to afford to pay for these treatments and scans out of pocket, and since the treatments are not FDA approved, in full. Insurance refused to cover my treatments because it is still considered to be an “experimental” procedure; however, I believe that if it were to be more affordable and accessible, it would benefit so many people that it would no longer need to be considered “experimental” and that it could be FDA approved and become a “normal” modern medicine procedure. This treatment quite literally saved my life and cured my chronic pain and if it were more affordable it could help an array of people suffering from a variety of chronic pain issues caused by an abundance of connective and soft tissue damage and disorders.

When most people go to their regular physician, at check out they pay a co-pay of, say, \$20 and their insurance covers the rest of their visit and any tests or scans done. When the FDA has not approved a medical treatment, it is much more difficult for a patient to get their insurance to pay for their treatment, as insurance companies do not want to “waste” their money on something they are not even sure will actually work. Because of this many families cannot afford prolotherapy and the tests and scans that come along with it, as it is so expensive to begin with. One DMX scan usually runs right around \$1,000 before any treatment, anesthesia, medicine, or other scans are added to the bill, and the procedure itself can cost anywhere from \$400 up (Ana Gotter, healthline.com).

No one wants to have joint hypermobility syndrome or Ehlers-Danlos syndrome, two connective tissue disorders that are treated by prolotherapy, much less pay thousands of dollars to have it treated and cured. With the approval by the FDA, prolotherapy will not only become more affordable but more accessible as people around the world suffer from these conditions and there are not many reputable prolotherapists. Many patients have to fly in and stay in a hotel, and sometimes Dr. Hauser will ask a family to live in Fort Myers for months to ensure full recovery and adequate healing time. FDA approval will make insurance coverage much more realistic and will make it easier for those suffering from these debilitating conditions to have the treatment they need to be able to go about daily life without chronic pain slowing them down or even stopping them.

### **Introduction to Prolotherapy**

Prolotherapy is a regenerative procedure that was designed to help those with soft tissue injuries to once again live a full life. Prolotherapy is the injection of 5-percent dextrose into joints with instability and/or torn or stretched ligaments. In my case, I had a torn labrum in my hip, severe cervical instability, and slight instability of my meniscus, a piece of cartilage that acts as a cushion between the thighbone and the shinbone, in my right knee. While getting prolotherapy, a patient can also receive platelet-rich plasma or bone marrow prolotherapy, among other things, in the same or different joints to help speed up the treatment and make it more effective.

Inflammation is defined as the body's reaction of vascularized living tissue to a local injury. Despite the importance of the body's natural inflammatory response in the healing process, non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to reduce or even

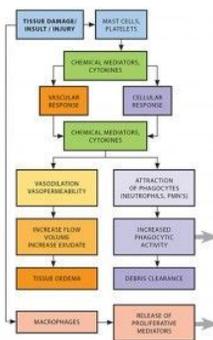
eliminate inflammation. This is because modern medicine tends to treat tendon and ligament injuries the same as muscle injuries. Because of the widespread use of NSAIDs to treat soft-tissue damage and injury, soft-tissue problems are rarely diagnosed, much less treated and helped. Prolotherapists take this problem and make their own solution that is unique to each patient.

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# The Biology of Prolotherapy

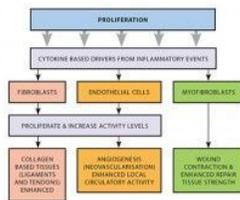
## Inflammatory Cascade.

After tissue damage by injury, the body attempts to heal the area by mediating this cascade. When the body is unable to heal itself, which is often the case when avascular (no or little blood supply) tissues such as ligaments, tendons, cartilage and fibrocartilage (meniscus and labrum) are injured, Prolotherapy is utilized to stimulate healing.



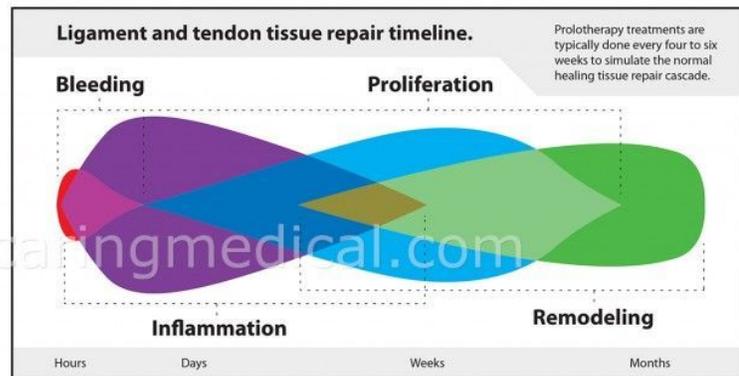
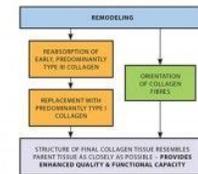
## Proliferation Cascade.

Prolotherapy stimulates healing via inflammation. After Prolotherapy solutions are injected into the injury site, a cellular reaction takes place in which various cells including fibroblasts, endothelial cells and myofibroblasts form new blood vessels and ultimately lay down collagen which enhances tissue repair and strength.



## Tissue Remodeling Cascade.

The final phase of healing is tissue remodeling. For many months after an injury or Prolotherapy, tissue continues to remodel. The new tissue that results looks and functions very closely to the original tissue before the injury. Once the tissue strength approaches that of the normal parent tissue, pain resolves.



Instability of the cervical spine is pervasive in Americans and according to Dr. Hauser in his book *Prolo Your Pain Away! Curing Chronic Pain with Prolotherapy*, “ligament weakness in the neck accounts for the majority of chronic headaches, neck, ear, and mouth pain” (69). The main stabilizing ligament of the facet joints (the meeting spot of two points of the vertebra) in the cervical spine (the neck), the capsular ligament, is a major source of chronic neck pain and

injury to this ligament causes elongation and laxity. Creep is the process of slow weakening of ligaments over time and this causes some ligaments to stretch up to 70% of their natural length. Cervical instability is seen on Digital Motion X-rays (DMX) or Functional MRI scans; however, there is no 100% sure test for cervical instability.

Joint hypermobility syndrome, according to Danielle Matias, MMS, PA-C in the Webinar titled “Joint hypermobility syndrome and joint instability with Prolotherapist Danielle Matias, MMS, PA-C” is a spectrum of people who are more “double-jointed” or flexible than the average person. While some people may only have one or two joints that are a little more flexible, others’ entire bodies may be hypermobile.

Prolotherapy is not approved by the FDA and is still considered an “experimental” procedure. The FDA should approve all Prolotherapy procedures because it not only can cure patients but change lives. The approval of Prolotherapy by the FDA would make getting insurance companies to pay for it easier and many more people could afford to have it done.

### **Conditions that Benefit from Prolotherapy**

There is an abundance of conditions that easily benefit from prolotherapy, among which are ligament laxity, joint hypermobility syndrome, also known as JHS, and Ehlers-Danlos Syndrome, also known as EDS. These conditions cause degeneration of soft tissue in joints and pain in joints. The laxity of ligaments caused by these conditions can also lead to muscle tension and pain and can ultimately cause more problems than what was initially diagnosed.

Ligament laxity is a general looseness of a joint that causes soft-tissue pain and can be a result of joint hypermobility syndrome or Ehlers-Danlos Syndrome. Joint instability can also stem from ligament laxity, joint hypermobility syndrome, and/or Ehlers-Danlos syndrome and

can be the cause of intense joint pain and muscle tension around the joint because the ligaments are not working as they should be.

Joint hypermobility syndrome is an extreme version of ligament laxity or joint instability, as it usually is diagnosed in people with multiple hypermobile joints or an entire hypermobile body. JHS is a hereditary connective tissue disorder and presents itself in an array of different clinical issues. The collagens (the primary constructive component of soft tissues) needed to create strong, tight ligaments and tendons affect the integrity of the ligaments in the joints in a negative manner due to their scarcity. It is rarely noticed by most physicians, as most modern medicine does not provide adequate training for examining and diagnosing problematic joint mobility and ligament laxity. Patients with JHS who have never been properly diagnosed or treated often experience severe chronic pain and joint hypermobility syndrome often leads to diffuse osteoarthritis. Some common signs of joint hypermobility, according to Dr. Hauser, are recurrent joint dislocations, frequent ankle sprains, a child with poor ball catching and handwriting skills, premature osteoarthritis, and laxity in other supporting tissues and structures (*Prolo Your Pain Away! Curing Chronic Pain with Prolotherapy* 219). This condition also leads to an increased risk of joint dislocations, temporomandibular disorders, pathologic disc degeneration, diffuse idiopathic skeletal hyperostosis, osteoarthritis, and joint injury during sports.

A study done at the University of Manchester of 125 children diagnosed with joint hypermobility syndrome showed that 74% of the children presented with arthralgia (severe pain). The study also showed that 13% of the children had speech difficulties, 14% learning difficulties, and 12% experienced urinary tract infection. 10% of the children showed subluxation (partial

joint dislocation) and/or full joint dislocations and 48% claimed to have limitations with school-based physical education activities. Finally, the study showed that 67% of the children examined had difficulties in activities other than physical education in school. A similar study also found a correlation between JHS and migraine headaches.

With prolotherapy, the loose ligaments and tendons involved in the instability are strengthened and tightened to restore stability to the joint. The people typically treated with prolotherapy who are diagnosed with joint hypermobility syndrome or simply joint instability are the ones who say something along the lines of “I’ve always been more flexible and I did some sport that is really hard on the body and now I’m 40 and I’m falling apart” (Dr. Danielle Matias, MMS, PA-C).

Ehlers-Danlos syndrome, also known as EDS, is a genetic, progressive, destructive ligament problem that is characterized by chronic pain caused by ligament laxity. The ligament laxity associated with this condition is due to defects in the biogenesis of collagen. The defect can be due to a parent who has the defect in their DNA or a genetic mutation during fetal development. While there is no clear and sure way to distinguish EDS from JHS, EDS is usually much more disabling and does cause fragility in the skin and can be the cause of excessive bruising after injury. EDS patients rarely respond well to orthopedic surgery but respond very well to, and can be cured by, prolotherapy. With EDS patients, the more unstable a joint is the less likely their joint instability and ligament laxity will respond well to orthopedic surgery, but the more likely they will respond well to prolotherapy.

### **How Prolotherapy Works**

Prolotherapy is an umbrella term used to refer to 5% Dextrose injections, Platelet-Rich Plasma injections, and many other types of therapy that use the body's natural inflammation process to encourage the body to heal itself. Inflammation is the body's way of healing soft tissue damage and injury, however many modern physicians treat soft tissue injury and pain the same way they would treat muscle injury and pain. This form of treatment ultimately causes the body to not be able to heal itself and pushes back the recovery process as long as anti-inflammatory drugs are being recommended and prescribed. Muscles can be treated with the RICE method. The RICE method is rest, which decreases joint nutrition, ice, which decreases blood flow, compression, which decreases pain control, and elevation, which causes incomplete soft tissue healing.

Alternatively, tendons and ligaments should be treated with the MEAT method. The MEAT method consists of movement, which increases joint nutrition, exercise, which increases blood flow, analgesic (acting to relieve pain), which increases pain control, and treatment, which encourages complete soft tissue healing. Healing is dependent upon the blood-supplying inflammatory cells to repair the damaged tissue, so consequently, poor blood flow reduces healing. Chronically weak tendons and ligaments are a result of deficient repair after an injury. Swelling after injury tells the body that there has been an injury in the body, which causes the immune system to send polymorphonuclear cells (cells that carry attack particles to release during infections, allergic reactions, and asthma) to the area. Then comes the fibroblastic stage of healing. Fibroblasts are the carpenters of the body and they form new collagen tissue, which is responsible for the strength of a ligament or tendon. This stage usually lasts from four to six weeks after the injury, so Prolotherapy is performed every four to six weeks to allow for

maximum time for soft-tissue growth. Finally, the maturation stage takes place and can last up to 18 months after the injury. During this phase, the collagen fibers formed in the fibroblastic stage increase in density and diameter. The increase in density and diameter can then result in increased strength in the soft-tissue.

Platelet-rich plasma, also referred to as PRP, prolotherapy is used to treat athletic injuries and tendinosis (a chronic condition that involves the deterioration of collagen in the tendons). To produce platelet-rich plasma with the lowest possibility of causing a reaction in the patient's body, blood is drawn from the patient and centrifuged, or "spun," to separate the different parts of the blood so the plasma can be extracted and used as a "glue" for the affected joints. This treatment puts blood cells into the joint and causes inflammation to encourage the body to heal itself, rather than needing surgery. This is especially effective in severe instability cases and can often lead to the patient needing fewer treatments. The use of platelet-rich plasma has gained popularity over the years, especially in treatment for sports injuries and tendon degeneration. According to Dr. Ross Hauser's *Curing Chronic Pain with Prolotherapy*, the platelets give off an abundance of growth factors and other bioactive substances that can contribute to the healing process. The use of platelet-rich plasma prolotherapy initiates and regulates the body's inflammatory response, which "promotes the migration, proliferation, and differentiation to mesenchymal and stromal repair cells to the area of injury" (45). The platelets in the plasma secrete growth factors and many other kinds of bioactive substances that can contribute to faster healing of soft tissue.

Bone marrow stem cell prolotherapy is used for bone repair and regeneration and the bone marrow is either put directly into the bone or is directed from the marrow to the bone.

Studies have shown improved treatment for nonunion fractures (the failure of healing following a broken bone unless intervened by surgery), avascular necrosis (the death of bone tissue due to a lack of blood supply), and spinal fusion with the use of bone marrow stem cells. Since the FDA has approved the use of bone marrow for use in orthopedics, there are many centrifugation machines that can be used to concentrate the bone marrow stem cells from plasma and red blood cells. Studies have also shown that the use of whole bone marrow in the fusion of nonunion fractures increased the fusion rate by 28% while using centrifuged marrow increased the fusion rate by 70%. Bone marrow has been used for the regeneration of bone, cartilage, and connective tissues. A human study has shown that bone marrow has the amount of MSCs and growth factors required for orthopedic medicine.

## **Conclusion**

In closing, the chronic pain and illness that come along with suffering from some of the least understood and diagnosed disorders are debilitating and take a large physical, mental, emotional, and financial toll on all who are involved with the patient. With approval from the FDA, prolotherapy would become more widely accepted and would increase the likelihood of coverage by insurance, making it more accessible and realistic for those who would not be able to afford it otherwise. This will make many lives feel worth living and could eliminate chronic pain caused by soft tissue damage and injury.

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