

Prolotherapy

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Prolotherapy is a method of injection treatment designed to stimulate healing.¹ This evidence-based treatment is used for musculoskeletal pain that has gone on longer than 8 weeks such as low back pain, sciatica, disc disease, neck pain, some types of headaches, chronic sprains and/or strains, whiplash injuries, tennis and golfer's elbow, knee, ankle, shoulder or other joint pain, chronic tendonitis/tendonosis, and musculoskeletal pain related to osteoarthritis. Prolotherapy works by raising growth factor levels or effectiveness to promote tissue repair or growth.² It can be used years after the initial pain or problem began, as long as the patient is healthy. Prolotherapy works to repair weak and painful joint areas and is a long-term solution rather than a palliative measure such as drug therapy.

Prolotherapy has been practiced in the United States since the 1930s, is endorsed by former U.S. Surgeon (1981–1989) General C. Everett Koop,³ and has made its way into major medical centers. In the April 2005 issue of the *Mayo Clinic Health Letter*, the authors wrote that in the case of chronic ligament or tendon pain that has not responded to prescribed exercise and physical therapy, prolotherapy may be helpful.⁴ Lloyd Saberski, MD, former Medical Director of Yale University School of Medicine Center for Pain Management, wrote that prolotherapy is the only methodology with limited risk yet potential for significant benefit.⁵ Prolotherapy has also

made its way into the professional sports world.⁵ One sports medicine journal reports:

Prolotherapy, considered an alternative therapy, is quietly establishing itself in mainstream medicine because of its almost irresistible draw for both physicians and patients: nonsurgical treatment for musculoskeletal conditions.⁶

The subject of prolotherapy has also been discussed in *The New York Times*, Personal Health column, where this author states: "Since prolotherapy is a nonsurgical technique, patients who are now facing surgery because all else has failed might consider it before having an operation."⁷ Yet many individuals, even physicians, may still know little about this treatment. The purpose of this chapter is to provide an introduction to prolotherapy, how and why it works, and indications for its use.

BACKGROUND AND HISTORY

Prolotherapy is based on the premise that chronic musculoskeletal pain is due to inadequate repair of fibrous connective tissue, resulting in ligament and tendon weakness or relaxation (laxity),¹ also known as connective tissue insufficiency.⁸ Ligament and tendon tissues have a poor blood supply, and therefore take longer to heal than other tissues. In fact, incomplete healing is common after an injury to those structures.^{9(p42),10} It has been estimated that the usual best result of a completed connective tissue repair process is a return to normal connective tissue length, but only 50% to 60% of preinjury tensile strength.¹¹ Over time, and multiple injuries, this can result in laxity and connective tissue insufficiency.² When the connective tissue is weak, there is insufficient tensile strength or tightness.¹² Load bearing then stimulates pain mechanoreceptors.⁶ As long as connective tissue remains functionally insufficient, these pain mechanoreceptors continue to fire with use.¹³ If laxity or tensile strength deficit is not corrected sufficiently to stop pain mechanoreceptor stimulation, chronic sprain or strain results.²

This is the problem that prolotherapy addresses, by stimulating growth factors to resume or initiate a connective tissue repair sequence that is incomplete or never started, repairing and strengthening lax ligaments and/or tendons, reducing or eliminating pain.

Historically, the use of concept of prolotherapy dates back to Hippocrates, who treated dislocated shoulders of soldiers on the battlefields with red-hot needle cautery to stabilize the joint. From 1835 to 1935, injection of sclerosing type agents was used for hernias to proliferate new

fibrous tissue. It was during the 1930s that George Hackett, a general surgeon, made an observation, while doing hernia surgery on patients previously treated with proliferant type therapy, that injections made (usually in error) at the junction of ligament and bone resulted in profuse proliferation of new tissue at this union.¹⁴ Hackett then spent many years developing and refining injection therapy for tendons and ligaments, publishing his research and text in 1956. He defined prolotherapy as the rehabilitation of an incompetent structure [ligament or tendon] by the generation of new cellular tissue and concluded that a joint is only as strong as its weakest ligament.¹ Prolotherapy is sometimes called “Regenerative Injection Therapy” (RIT), “Reconstructive Therapy,” “Non-Surgical Tendon, Ligament and Joint Reconstruction, or Growth Factor Stimulation Injection.”¹⁵

Sclerotherapy is an older, inaccurate term for prolotherapy, based on the original theory that scar formation was the treatment mechanism. However biopsy studies have not demonstrated scar formation with mechanical, inflammatory, or growth factor prolotherapy with the agents and concentrations currently in use.² Rather, studies have shown a proliferation of new, normal, thicker, and stronger connective tissue after prolotherapy injections.¹⁶

SOFT TISSUE HEALING

In addition to the inherent paucity of blood supply in ligament and tendon areas, interfering factors may decrease the body's healing response to injury. It is well known that smoking slows repair of collagen in connective tissue.¹⁷ Sleep issues are also important in healing as growth hormone, important for rebuilding of tissue, peaks during a normal sleep cycle. Poor nutrition can also be an issue with tissue repair. It is well known that vitamin C is necessary for the body to produce healthy collagen, a major component of connective tissues such as joint ligaments and tendons. Vitamin C is so important that prolonged deficiency causes scurvy, a disease where collagen production is defective and connective tissue breaks down.¹⁸ However, other micronutrients also play a role in tissue repair, and deficiencies may be involved in poor tissue repair. In repetitive trauma, another problem exists in that each individual trauma may be insufficient to provide enough stimulus to prompt complete healing, so that even minor injury may be enough to accumulate damage to the point of initiating chronic pain.² Another reason that has been suggested for incomplete healing is the use of anti-inflammatory medications immediately after an injury.¹⁹ Inflammation is a necessary component of soft tissue healing and the use of anti-inflammatory medication

for sports injuries has been questioned and remains controversial. In the January 2003 issue of *The Physician and Sportsmedicine*, a review article examined the physiology and healing of soft tissue injuries and concluded that the use of NSAIDs may interfere with healing and is questionable in treatment of musculoskeletal injuries.²⁰

MECHANISM OF ACTION AND RESEARCH STUDIES

Prolotherapy works by causing a temporary, low-grade inflammation at the site of ligament or tendon weakness (fibro-osseous junction), “tricking” the body into initialing a new healing cascade. Inflammation activates fibroblasts to the area, which synthesize precursors to mature collagen, reinforcing connective tissue.² It has been well-documented that direct exposure of fibroblasts to growth factors causes new cell growth and collagen deposition.²¹⁻²⁵ Inflammation creates secondary growth factor elevation.² This inflammatory stimulus raises the level of growth factors to resume or initiate a new connective tissue repair sequence to complete one which had prematurely aborted or never started.² Animal biopsy studies show ligament thickening, enlargement of the tendinosseous junction, and strengthening of the tendon or ligament after prolotherapy injections.^{26,27}

Over the years since the 1930s, studies and reports have demonstrated the effectiveness of injection prolotherapy for musculoskeletal complaints, including case reports, pilot, retrospective, open face prospective, and double-blind placebo controlled studies.²⁸⁻⁵¹

These studies have clearly indicated the effectiveness of prolotherapy in the treatment of chronic musculoskeletal pain arising from posttraumatic and degenerative changes in connective tissue such as ligaments, tendons, fascia, and intervertebral discs.⁵¹

Several studies are noteworthy. In a study of chronic low back patients treated with prolotherapy, biopsies of sacroiliac ligaments 3 months after treatment demonstrated a 60% increase in collagen fibril diameter, as well as decrease in pain and increased range of motion in subjects tested.⁵⁰ A double-blind animal study done at the University of Iowa showed significant increase in rabbit bone-ligament-bone junction strength and increase of collagen fibrils after proliferant injections.¹⁷

A 2005 study of elite rugby and soccer athletes with chronic groin pain preventing full sports participation showed the marked efficacy of prolotherapy. After an average of 2.8 treatments, 20 of 24 athletes reported no pain, and 22 were unrestricted with sports.⁵²

Knee injuries have been studied and shown to be successfully treated with prolotherapy. A study involving patients with significant knee ligament laxity and instability showed highly significant tightening of the cruciate and collateral ligaments measured by standard electrogoniometer

measurements, as well as subjective improvement in pain and increased activity level 9 months after treatment start.⁵³ A double-blind study by Reeves showed that injection prolotherapy resulted in elimination of ACL laxity by machine measurement in over 60% of patients with statistically significant improvement at 3-year follow-up, with a larger percentage experiencing reduction in pain, including improvement in symptoms of osteoarthritis even in those who tested loose.⁵⁴

The largest follow-up studies to date on the pain reducing effects of prolotherapy treatment involved 1,800 patients followed-up for more than 2 years and showed marked reduction in upper or lower body pain in 80% of subjects.⁵⁵ A review of the medical literature by the Florida Academy of Pain Medicine in 2001 analyzed the medical literature from 1937 to 2000, including case studies, retrospective, prospective, and animal studies. The calculated number of patients reported in those studied exceeded 530,000. Improvement in terms of return to work and previous functional/occupational activities was reported in 48 to 82% of patients, with reduction of pain up to 100%. The academy concluded that this injection treatment was effective as a type-specific treatment for posttraumatic degenerative, overuse, and painful conditions of the musculoskeletal system related to pathology of the connective tissue.³⁹

APPROPRIATE CANDIDATES FOR PROLOTHERAPY

In the Hackett, Hemwall, and Montgomery book on prolotherapy, which was one of the first texts on the subject, the authors write:

Criteria for Injection Therapy in New Patients:

1. Appropriate medical problem.
2. Desire for recovery.
3. No underlying medical conditions which would significantly interfere with healing.
4. Ability and willingness to follow instructions.
5. Willingness to report progress.
6. Willingness to receive painful injections in an effort to recover from injury.¹

These criteria are still true today. The problem must be an appropriate musculoskeletal problem. The patient needs to have the desire to get better, no known illness which could prevent healing, and willingness to follow instructions and to undergo injections. Illnesses that would prevent healing include autoimmune or immunodeficiency disorders, or active cancers, for example. Also, the patient should not be taking drugs that lower the immune system such as systemic corticosteroids or immune

suppressants. And because prolotherapy works to stimulate inflammation, patients should not be taking anti-inflammatory medication during treatment. In fact, as mentioned above, although frequently prescribed for musculoskeletal pain, use of NSAIDs may interfere with healing and is questionable in treatment of musculoskeletal injuries.⁵⁶

Age is not a factor, as long as the individual is healthy. It also does not matter how long the person has been in pain, or how long ago they injured themselves, again, as long as the person is in good, general health.

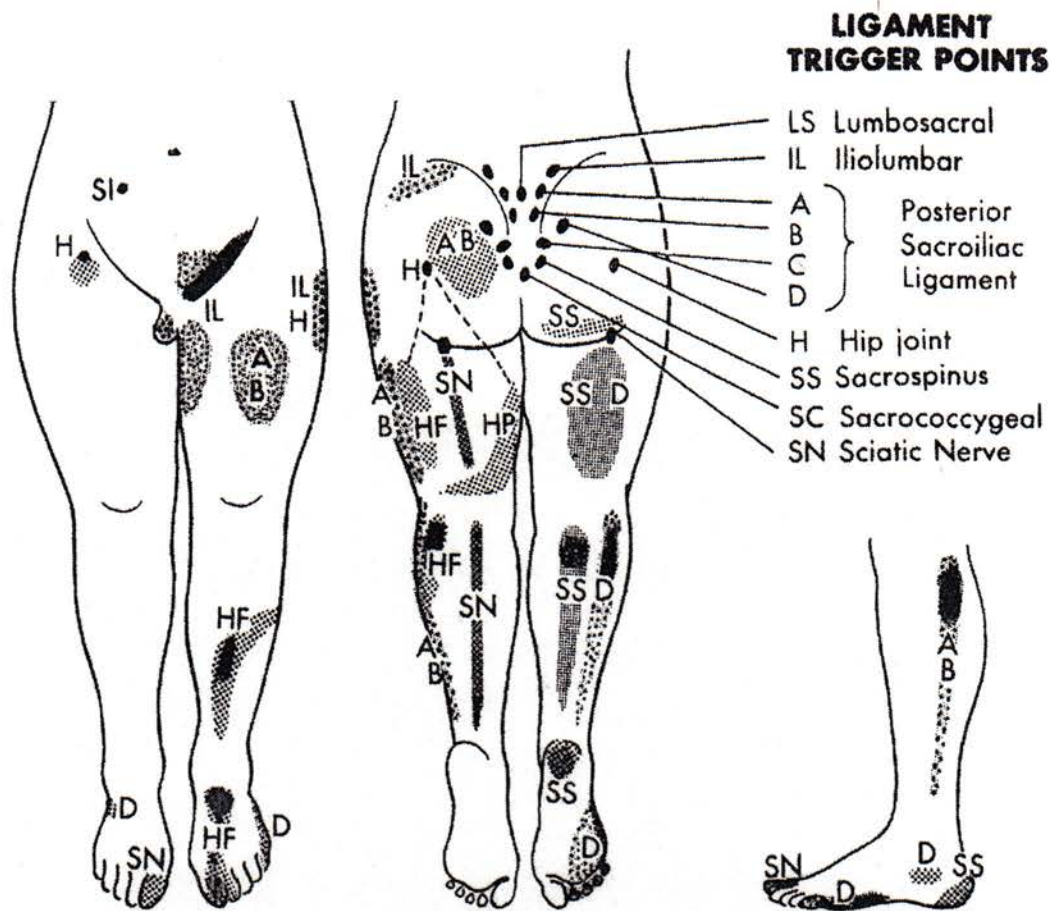
MRI STUDIES CAN BE MISLEADING IN DIAGNOSING MUSCULOSKELETAL PAIN

The Ombregt and ter Veer *Textbook of Orthopedic Medicine* states that the results of radiographic examinations should never be given as a diagnosis.^{57(p739)} As many health care practitioners know, an MRI may show nothing wrong and yet the patient is still in pain. And, because MRIs may also show abnormalities not related to a patient's current pain complaint, these MRI findings should always be correlated to the individual patient. Many studies have documented the fact that abnormal MRI findings exist in large groups of pain-free individuals.^{57(p59),58-63} A study published in the *New England Journal of Medicine* showed that out of 98 pain-free people, 64% had abnormal back scans.⁶⁴ Many other studies have also shown abnormal neck MRI scans in asymptomatic subjects,⁶⁵⁻⁶⁷ and the finding of asymptomatic changes in knee joints during surgery is not uncommon.^{68,69} One study looked at the value of MRIs in the treatment of knee injuries and concluded that, overall, magnetic resonance imaging diagnoses add little guidance to patient management and at times provide spurious [false] information. However, many surgeons base their decisions to operate primarily on the outcome of these investigations.^{57(p700)} It is inevitable, then, that some of the surgeries done are unnecessary and will not resolve the pain for which they are intended. So an MRI alone should not be used to determine a treatment course. The MRI should be used in combination with a history of the complaint, precipitating factors or trauma, and a physical exam.

PAIN REFERRAL PATTERNS

The concept of pain referral is not new in medicine. A tooth infection may cause ear pain; a heart attack may produce arm or jaw pain. Referral patterns also exist for injured joints, ligaments, and tendons. An important concept in musculoskeletal medicine is that of ligament referral patterns. Injury in

one part of the body can affect distant body parts.^{9(p46)} Ligament injury may cause severe pain because ligaments are full of nerve endings⁷⁰ and may refer nerve-like pain, making diagnosis difficult. Pain from sciatica, for instance, may actually be coming from injured sacroiliac or sacrospinous ligaments rather than the sciatic nerve (Figure 18.1), or musculoskeletal



PAIN REFERRAL PATTERNS FROM LUMBOSACRAL AND PELVIC JOINT LIGAMENTS

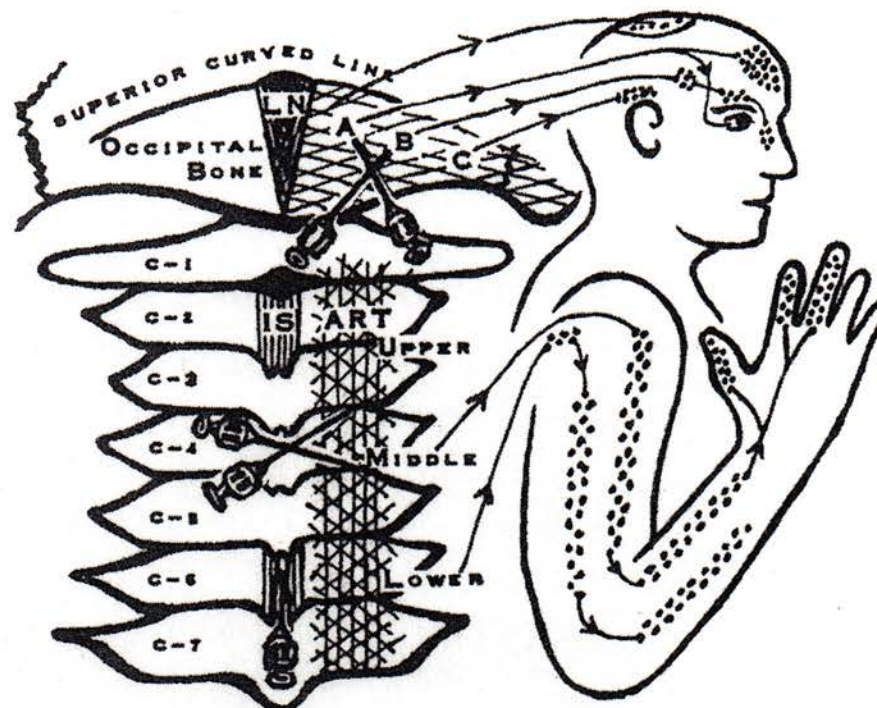
ABBREVIATION	LIGAMENT	REFERRAL PATTERN
IL:	ILIOLUMBAR	GROIN, TESTICLES, VAGINA, INNER THIGH
AB:	POSTERIOR SACROILIAC (UPPER TWO-THIRDS)	BUTTOCK, THIGH, LEG (OUTER SURFACE)
D:	POSTERIOR SACROILIAC (LOWER OUTER FIBERS)	THIGH, LEG (OUTER CALF) FOOT (LATERAL TOES)— ACCOMPANIED BY SCIATICA
HP:	HIP—PELVIC ATTACHMENT	THIGH—POSTERIOR & MEDIAL
HF:	HIP—FEMORAL ATTACHMENT	THIGH—POSTERIOR & LATERAL LOWER LEG—ANTERIOR & INTO THE BIG TOE & SECOND TOE
SS:	SACROSPINUS & SACROTUBERUS	THIGH—POSTERIOR LOWER LEG—POSTERIOR TO THE HEEL
SN:	SCIATIC NERVE	CAN RADIATE PAIN DOWN THE LEG

FIGURE 18.1 Ligament referral pain patterns.

headaches, which may be referring from weak cervical ligaments or occipital attachments (Figure 18.2). If the ligaments from which the pain is being referred are treated with prolotherapy, the ligaments heal, pain receptors stop firing, and this type of pain resolves. Therefore, knowledge of areas in which individual ligaments may produce referred pain is extremely valuable in diagnosis and treatment with prolotherapy.^{9(p38)}

TENDONITIS/TENDONOSIS

Tendonitis is defined as “an inflammatory condition of a tendon, usually resulting from strain.”⁷¹ If the condition has gone on longer than 6 weeks, it is sometimes called chronic tendonitis. However, biopsies of so-called



HEAD AND NECK REFERRAL PAIN PATTERNS LIGAMENT AND TENDON RELAXATION

AREA OF WEAKNESS

OCCIPUT AREA A

OCCIPUT AREA B

OCCIPUT AREA C

CERVICAL VERTEBRAE 1-3 (UPPER)

CERVICAL VERTEBRAE 4-5 (MIDDLE)

CERVICAL VERTEBRAE 6-7 (LOWER)

REFERRAL PATTERN

FOREHEAD AND EYE

TEMPLE, EYEBROW AND NOSE

ABOVE THE EAR

BACK OF NECK AND POSTERIOR SCAPULAR REGION (NOT SHOWN)

LATERAL ARM AND FOREARM INTO THE THUMB, INDEX
AND MIDDLE FINGER

MEDIAL ARM AND FOREARM INTO THE LATERAL HAND, RING
AND LITTLE FINGER

FIGURE 18.2 Head and neck ligament referral pain patterns.

chronic tendonitis tissue has shown lack of inflammatory cells and repair but rather collagen degeneration occurring.⁷²⁻⁷⁴ For this reason, in recent years the word *tendonosis* (*osis* meaning “diseased or abnormal condition”) is being used in the medical literature to describe what has previously been known as chronic tendonitis, which some authors believe may be a more accurate diagnosis. In this type of tendonopathy, inflammation is no longer occurring and collagen breakdown is the primary problem. Traditional treatments include NSAIDs and corticosteroids; however, studies provide little evidence that these treatments are helpful.⁷⁵ Therefore, treatment should target the stimulation of collagen production rather than the elimination of inflammation, which may not even be present.⁷⁶ Prolotherapy is a more reasonable treatment option in that the focus is to stimulate the proliferation of fibroblasts which then stimulate collagen repair and proliferation. The tendonosis is turned into a tendonitis (on purpose) in order to stimulate the repair process to start again.^{77(p92)}

LOW BACK PAIN

Low back is a common medical complaint. In the United States alone, more than 5 million people are disabled by low back pain, half of these permanently.⁷⁸ Low back pain affects most people at some point during their lifetimes. It is the second most frequently reported illness in industrialized countries, next to the common cold.⁷⁸ In fact, it has been reported that 80% of the general U.S. population will at some time suffer from low back pain, and 20% are suffering at any given time.^{79,80} It is the subject of numerous books, articles, and media reports. A variety of sports activities, such as gymnastics, football, weight lifting, rowing, golf, dance, tennis, baseball, basketball, and cycling, have been linked to low back pain.⁸¹ Nonathletes and athletes alike, however, can suffer from this condition.

CAUSES OF MUSCULOSKELETAL LOW BACK PAIN

Ninety percent of low back pain is mechanical. This type of low back pain is the result of overuse or straining, spraining, lifting, or bending that results in ligament sprains, muscle pulls, or disc herniations.⁸² Mechanical low back pain is the most common cause of work-related disability in persons under 45 years old.⁸³ While disc problems have gotten much of the credit for low back pain, ligament injury is a more important source of back pain.^{57(p775)} In fact, it has been reported that *only 4% of low back pain is due to a herniated disc.*⁸³

To understand why the disc has been given so much credit for low back pain, one has to understand some medical history. In 1934 researchers named Mixter and Barr became popular.⁸⁴ They focused attention on the disc, giving root to a popular theory; from that time forward, so-called disc disease has overshadowed ligaments' importance. Then, with the introduction of cat scanners (CT) in the 1970s, and the popularity of MRIs in the 1980s and 1990s, further attention was focused on the disc as the cause of low back pain—because discs are easily seen in these types of studies. On the other hand, ligament injury which involves very small micro-tears usually does not show up well on these investigations so have been largely overlooked.

Low back prolotherapy studies have shown improvement in treated groups^{38,85-87} including a randomized double-blind trial which showed statistically significant improvement in the treated group after 6 months.⁸⁸ A 2004 study showed improvement in two groups of chronic low back patients, treated with dextrose or saline injections (both can be used as proliferants). Both groups showed a statistically significant decrease in pain and disability scores at both 12 and 24 months follow-up.⁸⁹ Hackett himself reported on 543 chronic low back patients with ages ranging from 15 to 88, with duration of disability before treatment from 4 to 56 years. Hackett reported that 82% of these patients considered themselves cured over periods ranging up to 12 years of follow-up.²⁸ A recent study by Ross Hauser also shows statistically significant improvement in low back pain patients treated with prolotherapy.⁹⁰

WEAK SPINAL LIGAMENTS PRECEDE DISC HERNIATION

Weakening of the spinal ligaments precedes disc herniations.⁹¹ For a disc to herniate, there must first be a primary ligament weakness and a deteriorating disc.^{1(p9)} Disc degeneration has become so common that it is considered part of the normal aging process.^{57(p729)} In the natural course of aging a disc loses pliability and is less able to withstand normal pressures. Thus, it is more prone to having its outside edges become cracked or torn.⁹² If the pressure goes high enough, the fluid in the disc's center can leak through these cracks or fissures. This also leads to decreased disc height. In addition, the ligament that holds the disc in place becomes weakened. As a result, the joint becomes even more unstable and more likely to herniate (Figure 18.3). Ligaments hold the disc in place, so if the ligament weakens, the disc can more easily herniate through it. In fact, increased pressure in the disc together with increased ligament laxity is the perfect recipe for disc herniation.^{57(p745),93}

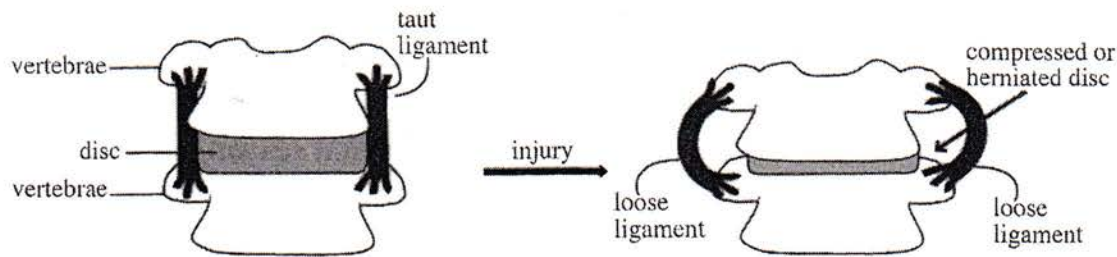


FIGURE 18.3 What happens to the ligament when the disc flattens.

SPINAL DISC DISEASE

Although initial onset of disc herniations is usually extremely painful and acute, in a few days to a few weeks the protruding disc segment slowly shrivels away.^{57(pp747,765)} In fact, with or without treatment, most disc herniations reabsorb and resolve within 2 to 6 weeks, with up to 90% back-to-normal activity within 1 month regardless of treatment.^{94,95} However, it has been estimated that 10% of people who suffer a disc herniation continue to have pain and go on to experience chronic back pain that includes muscle pain, spasm, and stiffness (a sign of a ligament laxity and a weak joint), sometimes with pain going down the legs. These symptoms may persist long after the disc herniation itself has shriveled away because of weakened back ligaments and connective tissue support which has not healed. Even after someone has “recovered” from a back injury or disc herniation to the point that he or she is out of severe pain, where ligaments are weak there still exists a predisposition to further injury. In addition to that, the change in biomechanics when a ligament weakens can contribute towards osteoarthritis in that joint as well as stress on other joints. Prolotherapy can help stabilize and strengthen the ligaments around these weakened joints and reduce or eliminate pain.

SCIATICA

Sciatica is defined as “pain emerging from the lower back that is felt along the distribution of the sciatic nerve in the lower extremity.”^{96(p1851)} A diagnosis of sciatica describes a symptom and is not specific in terms of cause. Frequently, the cause of sciatica is attributed to a finding on an MRI such as a disc herniation. However, for the majority of people who experience this type of pain, even in cases when numbness is present, the cause of the problem is not a disc but rather sacroiliac ligament weakness.⁹ In fact, it has been stated that ligament laxity in the sacroiliac joint is the number one reason for sciatica and is one of the most common reasons for chronic low back pain.⁹⁷

As discussed above, ligament referral patterns overlap nerve pathways. Note that the referral pattern for the sacroiliac ligaments are similar to those of the sciatic nerve (see Figure 18.1).

Piriformis syndrome is another often overlooked reason for sciatica, leg, or buttock pain.⁹⁸ The piriformis muscle tendon attaches directly over the exiting sciatic nerve. Injury, straining, or micro-tears to the piriformis tendon or other surrounding ligamentous structures result in inflammation and swelling, which puts pressure on the sciatic nerve, causing pain and referral.

A study by Merriman compared prolotherapy to fusion for sciatic pain, evaluating patients treated during his 40 years as a general and industrial surgeon. His conclusion was that conservative physiologic treatment by prolotherapy after a confirmed diagnosis of ligamentous and tendinous laxity was successful in 80% to 90% of more than 15,000 patients treated with prolotherapy, with fewer side effects than with fusion.⁹⁹

LIGAMENT INJURIES LEAD TO DEGENERATIVE ARTHRITIS

Osteoarthritis almost always begins as ligament weakness.⁷⁷ Unresolved ligament sprains (overstretching) results in ligament relaxation and weakness. Relaxation of the ligament results in joint instability and a change in joint biomechanics, which eventually results in osteoarthritis of that joint as bones glide over each other unevenly. The observation that bones remodel and grow in response to their mechanical environment is best explained in Wolff's Law which states: "Bones respond to stress by making new bone."^{100(p8)} Tendon injuries, if unresolved, over a long period of time also have an influence on joint biomechanics and can contribute to the development of osteoarthritis. In fact, *Postgraduate Medicine* reports in its investigation of the causes of arthritis: "There is no question that trauma and mechanical stress on the joint lead to the development of osteoarthritis."¹⁰¹

In veterinary medicine, it is well-established that ligament sprains also favor the development of osteoarthritis in animals.¹⁰² This has also been demonstrated in the human medical literature. One study of female soccer players who had sustained knee ligament injury showed a very high percentage with knee osteoarthritis 12 years later.¹⁰³ Another study, published in *Sports Medicine*, observed the increased incidence of arthritis with individuals who engaged in certain sports, for instance wrestlers, boxers, baseball pitchers, football players, ballet dancers, soccer players, weight lifters, cricket players, and gymnasts.¹⁰⁴

OSTEOARTHRITIS

In a recent double-blind placebo controlled study, there was clinically and statistically significant improvement in knee osteoarthritis symptoms at 1- and 3-year follow-up after prolotherapy injections, with radiographic readings also noting improvement in several measures of osteoarthritis severity. When present, ACL laxity also improved.¹⁰⁵ Another study showed improvement in finger and thumb osteoarthritis after prolotherapy injections, with 42% improvement in pain and 8 degree improvement in flexibility after 6 months.¹⁰⁶

If ligament and tendon injuries are stimulated to heal, this downward progression of degenerative changes can be prevented or stopped. Prolotherapy can, therefore, be seen as a method to prevent or stop the arthritic process because it strengthens the joint, thus ending the need for the knee or other treated joint, to grow bone or form bone spurs (Figure 18.4).⁷⁷

KNEE PAIN WHEN MRI SHOWS MENISCAL INJURY

Meniscal tears are a common diagnosis with knee pain, in part because MRIs clearly show these tears. However, as noted above, MRIs can be misleading, and this is especially true with the meniscus. A knee MRI study addressed this issue. The authors looked for meniscal abnormalities in asymptomatic, pain-free individuals aged 20s to 80s and found Grade 1, 2, and 3 changes present in essentially all decades, with an increase in prevalence with increasing age. 62% of individuals as young as their 20s had abnormal medial meniscal scans while 90% of these scans were abnormal for pain-free individuals in their 70s.¹⁰⁷

Another interesting note is that the medial meniscus firmly adheres to the deep surface of the medial collateral ligament (MCL), an important stabilizing ligament.¹⁰⁸ Therefore injury to the medial meniscus will very often also result in injury and sprain to the MCL. The cause of the knee pain may be the MCL sprain; however, MCL sprains are usually not addressed, especially if the MRI shows a meniscal tear. This could explain pain persisting after meniscal surgery. Clearly, the presence of meniscal tears on MRI needs to be correlated to an individual's pain complaint. Pain may not be related to the abnormal findings on an MRI but rather ligament or tendon injury or sprain/strain. In fact, individuals with abnormal MRIs showing meniscal tears have successfully been treated with prolotherapy. It is unclear whether prolotherapy has any direct effect on meniscal tissue, and this has not been specifically studied. However, even when patients have these meniscal abnormalities on MRI, they often improve after prolotherapy treatment.

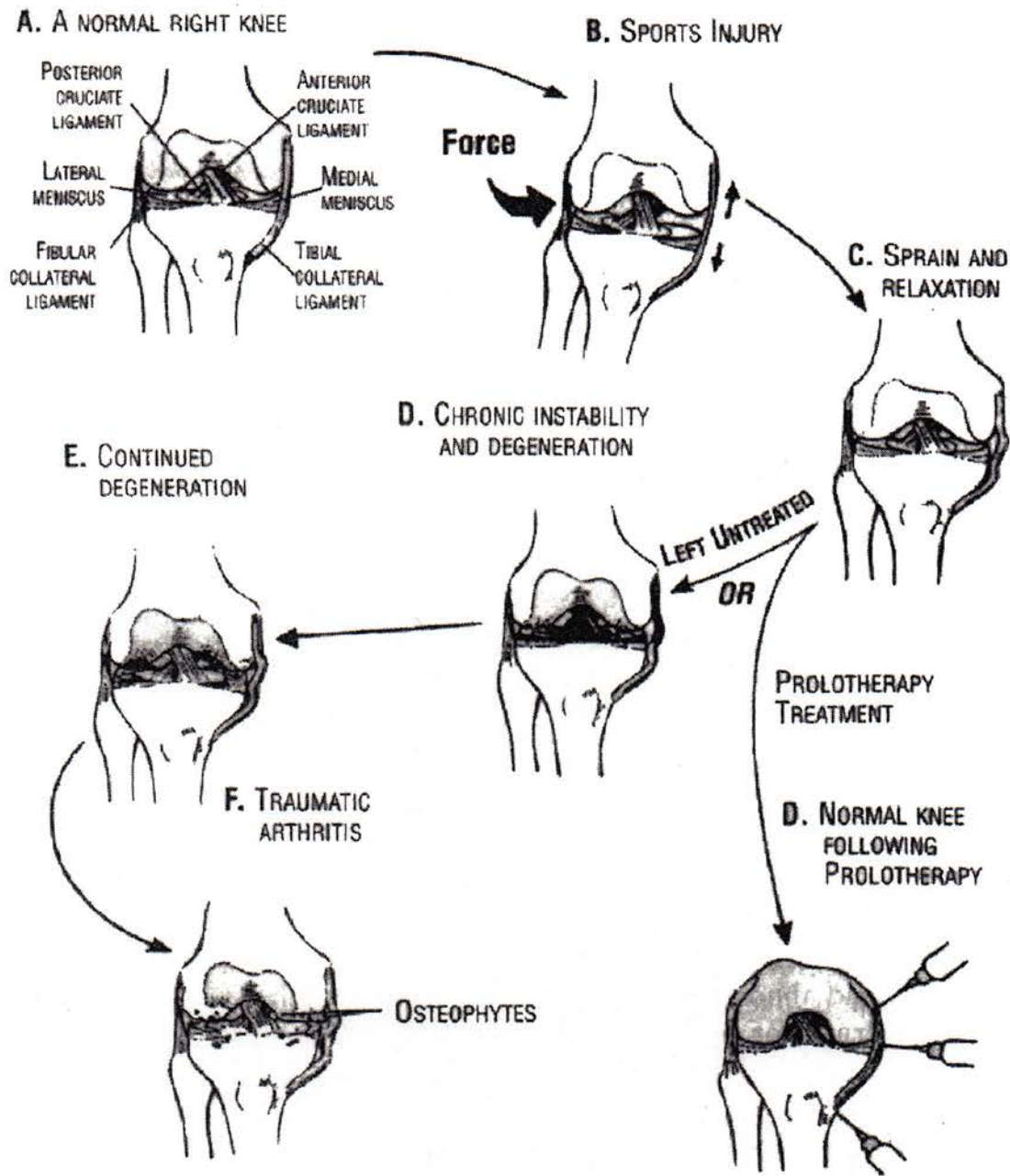


FIGURE 18.4 How soft tissue injury leads to degenerative arthritis. Ligaments become sprained following trauma. When healing does not occur, the ligaments become relaxed, resulting in chronic instability and degeneration from meniscal and articular cartilage degeneration. When left untreated, posttraumatic "arthritis" or degenerative osteoarthritis follows. This degenerative process can be prevented with appropriate intervention through prolotherapy.

CARTILAGE REGENERATION

An important issue in joint diseases is the difficulty in regenerating damaged articular cartilage, and therefore cartilage regeneration is one of the most preferred subjects for medical research investigation.¹⁰⁹ It has been suggested that prolotherapy may help in cartilage regeneration, however no specific controlled studies have yet been done to confirm this. Laboratory studies demonstrate cartilage cells respond to injury (inflammation) by changing into chondroblasts, cells capable of cell proliferation, growth, and healing.¹¹⁰ And although not studied in humans, cartilage effects of growth factor stimulation in animals has shown healing of full thickness cartilage defects and improvement of osteoarthritis lesions in injection studies.¹¹¹⁻¹¹³ Therefore, it has been suggested that prolotherapy might help in cartilage regeneration because of its ability to raise growth factor levels. A case report by Dr. Ross Hauser in Oak Park, Illinois, shows clinical evidence of such a change. X-rays were taken of a patient with severe arthritic degeneration were done before and after prolotherapy treatment, 1 year apart. Please note that it is difficult, if not impossible, to take two X-rays of the same joint and have them be exactly the same view and beam penetration, and this was not a formal study. However, it does raise an interesting question. The patient was a 62-year-old female who when first seen was unable to ambulate without a cane. After 12 prolotherapy sessions approximately 1 month apart, this patient was pain free with full mobility. Clearly, more clinical trials need to be done on the question of prolotherapy and cartilage regeneration, and this would be a good future area of investigation.

NECK PAIN AND MUSCULOSKELETAL HEADACHES

The optimal long-term, symptomatic therapy for chronic neck pain has been investigated for unresolved neck pain at a charity clinic in rural Illinois. Ninety-eight patients were followed on an average of 18 months after prolotherapy treatment. Prior to treatment, these patients had suffered with pain an average of 59 months. Some of the patients had been told by their doctors that there were no other treatment options or that surgery was their only answer for their chronic pain. Ninety-seven percent of patients reported some pain relief with prolotherapy. Ninety-one percent considered the prolotherapy treatment on them to be very successful (greater than 50% pain relief), and 90% of patients who were on medications at the start of prolotherapy treatment were able to curb their pain medication usage by 50% or more.⁹⁰

Headaches can have many different causes. In addition to musculoskeletal causes, there may be neurological, hormonal, allergic, or pathological causes for headaches that need to be addressed. If the cause of a headache is musculoskeletal, prolotherapy may be helpful since upper cervical ligament dysfunction may refer pain to the head (see Figure 18.2).

OTHER PAIN CONDITIONS

Prolotherapy has been used to successfully treat a large variety of musculoskeletal syndromes, including cervical, thoracic, and lumbar pain syndromes, patients diagnosed with disc disease, mechanical low back pain, plantar fasciitis, foot or ankle pain, chronic rotator cuff or bicipital tendonitis/tendonsis, lateral and medial epicondylitis, TMJ dysfunction, musculoskeletal pain related to osteoarthritis, and even finger or toe joint pain including so-called turf toe. It is important to rule out a systemic or nonmusculoskeletal origin for the complaints, confirm no underlying illness which would prevent healing, and also to ensure there are no contraindications to treatment (see section below).

The Florida Academy of Pain Management laid out indications for prolotherapy (regenerative injection therapy or RIT) based on their review of the literature:

1. Chronic pain from ligaments or tendons secondary to sprains or strains.
2. Pain from overuse or occupational conditions known as "Repetitive Motion Disorders," i.e., neck and wrist pain in typists and computer operators, "tennis" and "golfers" elbows and chronic supraspinatous tendinosis.
3. Chronic postural pain of the cervical, thoracic, lumbar and lumbosacral regions.
4. Painful recurrent somatic dysfunctions secondary to ligament laxity that improves temporarily with manipulation. Painful hypermobility and subluxation at given peripheral or spinal articulation(s) or mobile segment(s) accompanied by a restricted range of motion at reciprocal segment(s).
5. Thoracic and lumbar vertebral compression fractures with a wedge deformity that exert additional stress on the posterior ligamentotendinous complex.
6. Recurrent painful subluxations of ribs at the costotransverse, costovertebral and/or costosternal articulations.
7. Osteoarthritis of axial and peripheral joints, spondylosis, spondylosis and spondylolisthesis.

8. Painful cervical, thoracic, lumbar, lumbosacral and sacroiliac instability secondary to ligament laxity.
9. Intolerance to NSAIDs, steroids or opiates. RIT (Prolotherapy) may be the treatment of choice if the patient fails to improve after physical therapy, chiropractic or osteopathic manipulations, steroid injections or radiofrequency denervation or surgical interventions in the aforementioned conditions, or if such modalities are contraindicated.⁵¹

PROLIFERANT SOLUTIONS

The most common proliferant used in prolotherapy injections is hypertonic dextrose, 12.5% to 25%, with 15% being the most used. This is a safe solution which works by creating an osmotic gradient in the area of injection, dessicating the local connective tissue cells, initiating an injury response, and activating the inflammatory cascade. Once the cell fluid is able to dilute the dextrose, the inflammation ceases, however growth factor activation continues.¹⁶ A local anesthetic such as lidocaine or procaine is also used. Sarapin (extract of pitcher plant) is added in the Hackett-Hemwall-Hauser formula. A saline, rather than dextrose, based formula may also be used as a proliferant. Other solutions in use include noninflammatory dextrose (10% or less), which has been shown in two double-blind studies to be effective in both finger and knee arthritis and also improve knee ACL laxity and pain. Other, more inflammatory formulas in use are phenol-containing-solutions, such as P2G (phenol, glycerin, and dextrose).

CONTRAINDICATIONS

Active infection or cancer is a contraindication to treatment, as is any underlying illness that could interfere with healing. Immunodeficiency conditions, acute gout or rheumatoid arthritis, complete rupture of a tendon or ligament, nonreduced dislocations, or severe, unstable spondylolithesis are also contraindications. Other contraindications are allergy to any of the ingredients in the prolotherapy formula or unwillingness to experience possible after-treatment discomfort. Patients should understand the course of the prolotherapy treatment and be participants in their treatment plan.

Relative contraindications include current and long-term use of high doses of narcotics as these medications can lower the immune response. Current use of systemic corticosteroids or NSAIDs are also relative

contraindications as these are counter-productive to the inflammatory process. Other relative contraindications include central canal spinal stenosis and severe degenerative hip osteoarthritis with loss of range of motion.

RISKS

The most common risk is soreness after treatment. However, prolotherapy is a medical procedure, and as such there are risks. While prolotherapy is a low-risk procedure, any possible risk should always be fully discussed with a patient prior to treatment and a medical consent signed. Typical risks include bruising around the injected area and the risk of being in more pain, typically for 1 or 2 days after treatment because of the intended inflammation. However there is a risk that the pain after treatment will continue longer than expected. Other more rare risks include infection, headache, nerve irritation, allergy, puncture of an organ (such as the lungs) if injecting around that region, epidural puncture, or other unexpected risk. There is also the risk that the procedure will not work.

TYPICAL TREATMENT COURSE

Treatment intervals are spaced according to how that individual heals. On the average, the treatment interval is usually 3 to 4 weeks between treatments. In some people it is shorter, in others it is longer. The average number of treatments for any given area is usually between 4 and 6 total treatments, each treatment involving multiple injections to a particular area. Improvement is sometimes noticed after the initial treatment, however more often noticed by the second or third treatment. Some individuals require more than six treatments, and in some cases less treatments are needed. Individuals with hypermobility often take longer.

CONCLUSION

Prolotherapy is a reasonable and conservative approach to many different types of musculoskeletal pain, including back and neck pain; disc disease; headaches; chronic sprains and/or strains; whiplash injuries; tennis and golfer's elbow; knee pain including meniscal injuries; ankle, shoulder, or other joint pain; chronic tendonitis. It also may work in some aspects of cartilage regeneration. Prolotherapy is a treatment modality that provides a long-term solution rather than just palliation, and therefore should be considered in appropriate patients prior to long-term narcotic therapy or surgery in most cases.

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