What is prolotherapy?
Prolotherapy is used for musculoskeletal pain or injury which is either unresolved after eight weeks, or, if earlier, where enhanced healing is desired. Prolotherapy works by raising growth factor levels or effectiveness to promote tissue repair or growth. It can be used years after the initial pain or problem began, as long as the person is healthy. Because prolotherapy works to repair weak and painful joint areas, it is a long-term solution rather than a temporary measure such as drugs or corticosteroids.

How does prolotherapy work?
Prolotherapy works by causing a temporary, low grade inflammation at the injection site, activating fibroblasts to the area, which, in turn, synthesize precursors to mature collagen and thus reinforce connective tissue. It has been well documented that direct exposure of fibroblasts to growth factors (either endogenous or exogenous) causes new cell growth and collagen deposition. Inflammation creates secondary growth factor elevation. The inflammatory stimulus of prolotherapy raises the level of growth factors to resume or initiate a new connective tissue repair sequence which had prematurely aborted or never started. Biopsy studies show ligament thickening, enlargement of the tendinosseous junction, and strengthening of the tendon or ligament after prolotherapy injections. Prolotherapy injections are given in order to stimulate the body to repair painful injured areas.

How does prolotherapy differ from steroid injections?
Prolotherapy works through the process of inflammation. Contrary to popular belief, inflammation is actually a good thing. Inflammation is the process by which the body heals. Traditional treatments such as NSAID (non-steroidal anti-inflammatory) medications, cortisone shots, and ice actually stop the healing process. Prolotherapy injections are given at the point(s) where the ligaments and tendons attach to the bone(s) also known as the fibro osseous junction. A “proliferant” solution is injected into the injured area, stimulating the body to send healing cells to the injection sites. When the cells arrive to the injured area, they cause a localized inflammatory reaction and the patient will see swelling in the injected area. With this come healing immune cells that allow the body to lay down new tissue growing thicker, stronger ligaments and tendons.
**Does injection technique differ from standard steroid injections versus prolotherapy?**

One of the key points to treating pain and injury is to realize that most injuries and musculoskeletal pain symptoms, even degenerative arthritis, arise due to joint instability. Why are the joints unstable? It is because the ligaments and tendons holding the joints together are weak or loose (laxity). If this looseness is not treated, the joints remain unstable. To resolve the pain, the patient requires joint stabilization therapy, otherwise known as Comprehensive Prolotherapy.

Most people do not want to receive a lot of injections. Injections can be painful. However, if you want to achieve a curative result with prolotherapy, there must be a comprehensive approach to treatment. Injecting all of the injured structures (i.e. not just the joint, but also the surrounding support structures) using a strong enough proliferant (prolotherapy solution).

Most people understand, conceptually, that if you injure a structure in a joint that over time that injury will affect all the structures of the joint. Most patients come to see a prolotherapy specialist after having pain for at least several years. What may have started out as a simple ligament sprain, after 3-6 years, is now a total joint problem. All the structures of the joint and around the joint (or at least the majority of them) must be treated with prolotherapy to completely alleviate the pain.

**What type of solution is injected in prolotherapy?**

Prolotherapy involves the injection of orthobiologics, which are substances designed to induce healing in the body. There are two types of orthobiologics, those that come from the body (cellular), such as platelet rich plasma (PRP) and stem cells (bone marrow and fat), and those that naturally induce healing such as dextrose (which is chemically identical to d-glucose in the body). Cellular Prolotherapy involves the injection of orthobiologics that come from the patient’s own body such as PRP and stem cells. The reason this type of Prolotherapy is used is because the pain is caused from a cellular deficiency such as bone on bone arthritis, where for example, a deficiency of cartilage cells exists. Comprehensive dextrose Prolotherapy involves the injection of natural substances such as dextrose, which is d-glucose or the normal substrate used by almost all cells of the body for energy. Valley providers do not offer prolotherapy injections using dextrose.
What conditions are treated with Prolotherapy?
Prolotherapy is used in the field of musculoskeletal or orthopedic medicine to treat musculoskeletal conditions where the origin of the painful condition is related to an underlying instability or looseness of the ligaments and tendons, or where a deficiency in cartilage exists. Prolotherapy has been successfully used to treat a wide array of conditions including but not limited to the following:

- **Knee Pain:** arthritis, meniscus tears, chondromalacia patella, runner’s knee, ACL/MCL tears
- **Back Pain:** post-surgical pain, alternative to laminectomy, degenerative disc disease, arthritis
- **Neck Pain:** headaches, disc problems, cervical instability, osteoarthritis, pinched nerves, chronic muscle spasms
- **Shoulder Pain:** labral tears, impingement syndrome, frozen shoulder, osteoarthritis, post fracture, bursitis
- **Hip Pain:** degenerative joint disease, labral tears, osteoarthritis, avascular necrosis, post hip fracture pain, bursitis
- **Ankle & Foot Pain:** strains or sprains, chronic ankle sprains, plantar fasciitis, heel spurs, Morton’s neuroma, tarsal tunnel syndrome, Achilles tendinosis or tendinitis
- **Wrist Pain:** carpal tunnel syndrome, overuse injuries, sports injuries, strains, sprains, tendonitis, bursitis
- **Elbow Pain:** tennis or golfer’s elbow, tendonitis, osteoarthritis, strains and sprains
- **Body pain:** Ehler’s Danlos, Congenital hypermobility syndrome, fibromyalgia

Why is Prolotherapy not used more frequently for pain and sports injuries?
Although this treatment option has been around for many years, it is still considered by many to be an “alternative” treatment option for pain and injury because mainstream medicine still does not fully recognize it as a treatment option for soft tissue injuries. That being said, more and more practitioners are adding it to their medical practices and are using it with a high degree of success for relieving pain and injury in many patients, often with cure rates upwards of 80-90%, in the hands of a skilled prolotherapy practitioner.
**Patient Selection Criteria**

**Chronic tendinopathies (tendinosis and/or partial tear)**
- Pain duration longer than >3-6 months
- Symptoms and physical exam results consistent with tendinopathy, osteoarthritis
- Relcalcitrant to standard nonoperative treatment (physical therapy, NSAIDs, activity modification)
- Tendiopathic changes on diagnostic imaging: MRI or ultrasound
- Patient wishes to pursue alternative to surgical debridement
- No contraindications to the procedure exist (infection, coagulopathy or anticoagulants)

**Treatment after PRP**
- Physical therapy - eccentric strength training approximately 2-3 weeks after PRP injection (after the inflammatory stage of the healing cascade)

**Acute myotendinous injury and/or ligamentous injury**
- Acute injury (7-10 days)
- Symptoms consistent with myotendinous injury at the enthesis, musculotendinous junction, or muscle strain or partial tear or ligament injury grade 1-2
- Partial tear documented on imaging: MRI or ultrasound
- No contraindications to the procedure exist (infection, coagulopathy or anticoagulants)

**What is the ideal time to administer PRP?**
Patients who have not responded well to a comprehensive trial (3-6 months) of standard management and rehabilitation of a sports injury, are functionally impaired, with a pain score higher than a 4 out of 10 on a 0-10 visual analog scale. The patient will need to be out of play during the initial painful and post procedure period. Return to sports is variable, ranging from 4 weeks to 3 months, depending on the severity of the injury, chronicity of symptoms, other medical or orthopedic comorbidities, and level and type of sports participation and type of injection performed.

**What is the ideal number of injections performed?**
Valley providers begin with one injection and have the patient return in 6-8 weeks. If the improvement is 80% or greater, then Valley's providers defer further injections. If the improvement is less than 80% and the patient would like to achieve further gains, then a second injection will be offered. The time between injections is 6-8 weeks.
What activities should be avoided during the intervals?
Activity progression and post procedure pain is variable. There is typically a range of 2-10 days for the post procedure pain to subside. Initiate range of motion as soon as tolerated. The patient will then progress to light aerobic activity as tolerated within 3-7 days. Strengthening and sports specific training in 3-4 weeks.

What anatomic structures should be targeted and how should they be targeted?
Valley's providers routinely use musculoskeletal ultrasound guidance for injections to target specific areas that require treatment. Target areas to treat may include abnormalities within the ligament and/or tendon or abnormalities at the entheses. Sonographic appearance, clinical correlation and sonopalpation are all important. Valley's providers use a peppering technique with several needle passes to target not only the local pathology, but also the surrounding tissues as well. This may include the enthesis, peritendon, intratendinous, myotendinous junction, intramuscular, ligament or intra-articular areas.

Should NSAIDs, systemic steroids or immunosuppressive medications be withheld? If so, for how long?
It is advised that the patient withhold NSAIDs for at least 10 days and preferably 3-6 weeks after a procedure. NSAIDs will inhibit the prostaglandin pathway and may reduce the beneficial effects stimulated by the release of the growth factors from the delivered platelets. This would interrupt the inflammatory phase of the healing cascade. Theoretically, use of NSAIDs may impede or delay healing and may even produce fibrosis. Patients who are taking systemic steroids or immunosuppressive agents are generally not offered PRP treatments. However this can be reviewed on a case by case basis.

What are the return to play outcomes that may be achievable with PRP and is there a role in the management of acute injuries in professional athletes?
Return to play may be 2-3 weeks earlier than expected based on clinical outcome studies.

Is there a separate mechanism for pain modulation distinct from the tissue healing?
There are some patients with chronic musculoskeletal conditions that have experienced complete pain relief within a few days after the injection. It is postulated that this may be a result of the release of serotonin form the platelet dense granules which have pain modulating effects. However since serotonin has a short half-life, the effect is usually not sustained.
**Do the injections hurt?**
Injections that pierce through the skin are obviously going to produce some pain. So, yes, prolotherapy injections can be painful. Every person comes with their own perceptions and ideas about pain. Some people can receive many injections and not move a muscle, where others feel pain just by looking at a needle! Most prolotherapy patients say that the pain from the prolotherapy injections does not compare to the pain the chronic pain patient experiences every day.

In order to help those who find prolotherapy injections difficult to bear, prolotherapy doctors will prescribe oral medications such as Tylenol with codeine or Vicodin to be taken prior to receiving prolotherapy treatments.

**Does insurance cover Prolotherapy?**
Insurance coverage of prolotherapy varies among insurance carriers. Medicare does not cover prolotherapy, therefore, unfortunately, a number of insurance carriers will also decide not to cover prolotherapy. Some insurance carriers will provide at least partial coverage. When evaluating whether to pursue prolotherapy for your pain or injury, please realize that it is often less expensive to pay out-of-pocket for prolotherapy, compared to paying co-pays (sometimes upwards of 30-50%) of very expensive surgeries, hospitalizations, and resultant rehabilitation.