

ined 81 patients with chronic low back pain.⁷ The 40 who received prolotherapy reported the greatest reduction in pain and disability scores after 6 months. A more recent trial from the Kansas Medical Centre showed similar results for knee arthritis.⁸ Patients here had greater reductions in pain while walking, had fewer episodes of knee buckling and gained a greater range of motion than did those who received placebo injections. The results of all 5 studies may be explained in terms of variance in patient selection, underlying pathology, social circumstances, additional therapeutic modalities or insufficient power of the study. Further research is needed to determine which components of the regimens are most effective and whether there are subgroups of patients who are more likely to respond to these safe treatments.

Modern prolotherapy evolved from an injection technique called sclerotherapy, which was first used in the 1920's to treat hernias and hemorrhoids. In the 1940's Earl Gedney, a well-known osteopath at the Philadelphia College of Osteopathic Medicine began to use sclerotherapy for back-related ailments. It was George S. Hackett an M.D. from Canton, Ohio who first coined the term "prolotherapy" in the 1950's. His book *Ligament and Tendon Relaxation Treated by Prolotherapy* continues to be used as a basic training reference.¹²

When ligaments and tendons are stretched, torn or fragmented, joints become painful. Traditional approaches with anti-inflammatory drugs and surgery often fail to stabilize the joint and relieve pain permanently. Prolotherapy has the unique ability to directly address the cause of instability and repair the weakened sites, resulting in permanent stabilization of the joint. When precisely injected into the site of pain or injury, prolotherapy creates a controlled inflammation that stimulates the body to lay down new tendon or ligament fibers resulting in a strengthening of the weakened structure. When the joint becomes stronger, pain relief might be an expected outcome.

Prolotherapy is a treatment technique involving the injection of growth factors or growth-factor-production stimulants to promote growth and repair of normal cells and tissue.¹³ Growth factors are complex polypeptides that initiate multiplication of new cells or reparative changes in current cells. The most commonly used but least studied solution for prolotherapy is P2G (2.5% phenol, 25% glucose, 25% glycerine). Human cells begin to produce growth factors within minutes to several hours after exposure to an extra cellular D-glucose (dextrose) concentration of as little as 0.6% (normal cellular glucose concentration is 0.1%).¹⁴ These growth factors include platelet-derived growth factor,¹⁵ transforming growth factor beta,¹⁶ epidermal growth factor,¹⁷ basic fibroblast growth factor,¹⁸ insulin-like growth factor¹⁹ and connective tissue growth factor. These growth factors have also been identified as key stimulants of tendon, ligament, and cartilage (not bone) repair and growth.²⁰

Regenerative Injection Therapy has been scientifically observed to increase the size of tendons and ligaments up to 40%. It has also been shown to increase

their tensile strength by as much as 200%. No scar tissue is formed (as would be the case in surgical procedures). The tissue formed from Prolotherapy is healthy, strong, flexible ligament or tendon tissue. Once the ligament or tendon has been repaired by prolotherapy, the nerves are no longer stretched or irritated.

The therapy involves injecting a solution of concentrated dextrose or another solution usually with local anesthetic into ligament or tendon attachments to bone. The solution is referred to as a "proliferating agent" because it produces a "proliferation of inflammation" in the injured area. This happens when macrophages rush to respond to the inflammation, stimulating a natural healing response and promoting growth factors in the cells of the affected tendons and ligaments. Fibroblasts lay down new fibrous tissue wherever they detect damage, while other natural substances trigger the growth of new blood vessels and the flow of nutrients. This localized inflammation increases the blood supply and flow of nutrients and stimulates the tissue to repair itself. Tissue healing is regulated by a complex growth factor network as demonstrated in a model of injury involving rabbit knee medial and anterior cruciate in-vitro cultures. Although both MCL and ACL collagen synthesis was increased by 160% over controls by the application of transforming growth factor beta 1, their response to epidermal growth factor was different.²¹

Each person's response to prolotherapy is different. The average number of treatments needed ranges from four to six. An injection is painful and depending on the proliferant (stimulant) used and the specific needs of the patient, some require sedation or pain medication to undergo the treatment. As treatment progresses, the injections become less painful to receive. Mild swelling and joint stiffness may be experienced after prolotherapy injections. Over-the-counter anti-inflammatory medications are avoided if possible because they are thought to lessen the inflammatory response and the benefit of therapy. Heat rather than ice may also be beneficial.

With the use of P2G, most people will require analgesic medication after their treatment. It is normal to experience muscle soreness for a few weeks after the treatment. This is most noticeable for the first two days after injection. There is a "window period" of about two weeks as inflammation subsides but healing of the ligament is not complete. During this period there may be a return of some of the original pain. Starting around four weeks after a treatment, ligament strengthening is occurring and about 75% of the benefit of the injection is noted. Re-evaluation and treatment is scheduled at six weeks because it takes approximately six weeks for 100% of the benefit of the treatment to be realized.

When considering the risks associated with RIT, a recent retrospective postal survey of practitioners of prolotherapy for back and neck pain in the United States and Canada is the best and most recent evidence available. Surveys were mailed to members of the American Academy of Orthopedic Medicine (AAOM) and the American College of Osteopathic Pain Management and