

Prolotherapy for patients with musculoskeletal disorders? Practical answers to your clinical questions. (Musculoskeletal Q & A).

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What is **prolotherapy** and what are the indications and contraindications for it? How is it applied? Why is it controversial?

Prolotherapy is injection of any substance that promotes growth of normal cells, tissues, or organs. Injection of the hormone erythropoietin to produce red blood cells is widely used, and a number of other substances have been used for treatment of patients with various medical disorders. This discussion focuses on **prolotherapy** for musculoskeletal disorders, including arthritis and back pain.

Noninflammatory growth factor production methods have been used in the treatment of patients with arthritis. Injection of a subinflammatory level of dextrose (10%) into the joints of patients with knee or finger osteoarthritis (OA) has been shown to be effective in improving pain or disease severity. (1-3)

Dextrose can create growth without inflammation. Research on a variety of human cells exposed to as little as 0.3% to 0.6% dextrose (the normal cell has 0.1% dextrose) indicates that within minutes to several hours the cells begin to produce growth factors, such as platelet-derived growth factor, transforming growth factor-beta, epidermal growth factor, basic fibroblast growth factor, and connective tissue growth factor. Note that both fibroblasts and cartilage cells respond to a variety of growth factors, which are often named for the first cell in which they are discovered but usually act on a variety of cells.

Studies on noninflammatory dextrose injection show significant findings. The knee OA study (111 knees injected with less than an ounce of dextrose divided among 3 injections) demonstrated a flexion improvement of 130,65% reduction in knee buckling, and significantly better effect than placebo ($P = .015$). (1) The finger OA study was smaller in patient number but showed improvement in pain with finger movement compared with placebo (42% vs 15%, $P = .027$) and a superior improvement in range of motion ($P = .003$) with 3 milliliters of dextrose divided among 3 injections over 6 months. (2)

Inflammatory **prolotherapy** is probably less expensive. However, all double-blind studies of this form had significant limitations. Two studies used multiple treatments concurrently and compared an inflammatory with a noninflammatory solution, which in itself may affect blinding. In a third study, the results were in such opposition to all previous results that it raised the possibility of flaws in technique. Difficulty in reproduction of technique was an issue in all of these studies because they were done with multiple injection sites in patients who had low back pain. In addition, a large-gauge needle was used to inject bony attachments, and irritation of structures by a needle has a potential therapeutic effect on its own.

Because the primary pathology in sprain and strain is in connective tissue, with secondary trigger points in muscle, correcting the primary pathology requires injection of the connective tissue. In arthritis, there is much to learn about the balance of disrepair and growth factors, but stimulation of growth factors has much to offer. Studies of noninflammatory **prolotherapy** show probable benefit in OA and possible benefit in ligament laxity. In addition, physicians performing acupuncture or muscle trigger point injection generally find **prolotherapy** more potent in managing chronic pain.

To learn **prolotherapy**, a physician interested in sports medicine essentially must learn the trigger points in ligaments and tendons and how to inject them. When this skill is mastered, the physician can keep up with advances in available proliferant solutions. What the physician injects will change as the literature progresses and may include different growth factors or growth factor stimulants or inflammatory agents.

Prolotherapy is controversial because physicians often use an antiquated definition, such as inflammatory injection to create growth and repair. In reality, many noninflammatory substances are capable of creating a rise in growth factors sufficient to cause proliferation of cells or tissues. Injection to create growth of cells is currently being used in all major hospitals in the United States.

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(2.) Reeves KD, Hassenein K. Randomized, prospective, placebo-controlled double blind study of dextrose prolotherapy for osteoarthritic thumb and finger (DIP, PIP, and trapeziometacarpal) joints: evidence of clinical efficacy. *J Altern complement Med.* 2000; 6:311-320.

(3.) Reeves KD. Prolotherapy: basic science, clinical studies, and technique. In: Lennard TA, ed. *Pain Procedures in Clinical Practice*. 2nd ed. Philadelphia: Henley and Belfus; 2000:172-190.

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