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To the Editor:

Re: Yelland MJ, Glasziou PP, Bogduk N, et al. Prolotherapy injections, saline injections, and exercises for chronic low-back pain: a randomized study. Spine. 2003;29:9–16

Professor Yelland and associates deserve appreciation for the enormous effort involved in performing their randomized clinical trial of prolotherapy. Their conclusion that "significant reduction in low back pain occurs with ligament injections irrespective of the solution injected" is consistent with previous studies. However, the study's methodology limited the power and accuracy of their conclusions regarding prolotherapy as being no more effective than saline injections.

The reasons why studies involving needling of entheses should never purport to be placebo controlled are becoming biochemically more clear. They are as follows:

1. Needling results in cell membrane disruption with release of lipids, which are naturally inflammatory and serve as signals for macrophage and fibroblast activity.

2. Microbleeding from injection results in elevation of growth factors for connective tissue growth. A study by Taylor *et al* have shown that injection of normal rabbit patellar tendons on just one occasion with autologous blood (0.15 mL) resulted in a stronger and histologically normal tendon.[1] A recent study by Edwards and Calandruccio showed that just one injection of autologous blood in patients with usual-care-resistant tennis elbow showed striking improvements.(2)

AQ: 1

Probable reasons for limited magnitude of benefit in this study include the following:

1. Solution was injected at an average of only 7 sites at each treatment, compared to injection of at least 30 to 40 sites in previous studies.[3,4] The important deeper interosseous sacroiliac ligaments were not injected by Dr. Yelland for the first four treatments. These are considered vital areas for initial injection in this region. There also was apparently no attempt made to inject the apophyseal joint capsules. These are also usually injected at the time of first treatment. Not injecting the primary nociceptive source can lead to a pain flare instead of benefit.

2. As much as 3 mL was injected at each site. Our experience has been that excess volumes injected in one location may lead to pain flare as well.

3. Patients were not sedated for injection. This limited the ability of the treating physician to probe to be more certain of sites injected and limited the amount of needle trauma with its additional proliferant effect.

4. The solution used had an osmolarity of approximately 1,062 *versus* approximately 2,100 in previous studies, with less osmotic shock effects expected, and less connective tissue proliferation.

Dr. Loeser's comments that this study "met all the criteria for excellence and did not have hidden flaws" are quite incorrect for the reasons above and quite far reaching for someone who does not perform the technique. Now that there are courses available in low back injection with cadaver and video use, which offer carefully programed training, there should be no reason to have this type of methodologic issues (*www.aaomed.org*). No instructor in the American Academy of Orthopedic medicine would instruct in the manner of injection in this study. It is a tremendous effort to do a clinical study, and with that amount of effort and expense in a complicated area like the low back, it especially calls for agreement about effective methodology. We suggest that, if the treatment effect is to be determined, a near-placebo is vital, such as skin puncture with subcutaneous or muscular injection without approaching entheses or bone surface. In addition, if the magnitude of benefit of prolotherapy is to be demonstrated, more attention needs to be paid to injection technique and volumes.

It should also not be overlooked that basic science studies have indicated that even different ligaments in or about the same joint respond differently to the same growth factors.[5] For example, although this low back study as conducted was not indicative of a dextrose effect, two double-blind placebo-controlled studies have shown significant benefit of noninflammatory dextrose in knee and finger arthritis.[6,7] Dextrose has also been shown to tighten loose anterior cruciate ligament ligaments by machine measurement.[8] Cellular exposure to dextrose results in elevation of levels of multiple connective tissue growth factors within minutes to hours. This fact alone should make us more than a little stubborn to continue researching this safe, gentle, and inexpensive substance.

Prolotherapy of connective tissue, whether with primary growth factors or with growth factor stimulants, is an exciting area of treatment and research. We will need to pull together as scientist, and hang on for the ride into evidence-based treatment of soft tissue conditions.[2]

AQ: 2

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References

1. Taylor MA, Norman TL, Clovis NB, et al. The response of rabbit patellar tendons after autologous blood injection. *Med Sci Sports Exerc*. 2002;34:70–73.
2. Edwards SG, Calandruccio JH. Autologous blood injections for refractory lateral epicondylitis. *J Hand Surg Am*. 2003;28:272–278.
3. Ongley MJ, Klein RG, Dorman TA, et al. A new approach to the treatment of chronic low back pain. *Lancet*. 1987;2:143–146.
4. Klein RG, Eek BC, DeLong WB, et al. A randomized double-blind trial of dextrose-glycerine-phenol injections for chronic low back pain. *J Spinal Disord*. 1993;6:23–33.
5. Scherping SC Jr, Schmidt CC, Georgescu HI, et al. Effect of growth factors on the proliferation of ligament fibroblasts from skeletally mature rabbits: effect of growth factors on the proliferation of ligament fibroblasts from skeletally mature rabbits. *Connect Tissue Res*. 1997;36:1–8.

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6. Reeves KD, Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. *Alt Ther Health Med*. 2000;6:68–80.
7. Reeves KD, Hassanein K. Randomized prospective placebo-controlled double-blind study of dextrose prolotherapy for osteoarthritic thumbs, fingers (DIP, PIP, trapeziometacarpal joints): evidence of clinical efficacy. *J Alt Compl Med*. 2000;6:311–320.
8. Reeves KD, Hassanein K. Long term effects of dextrose prolotherapy for anterior cruciate ligament laxity: a prospective and consecutive patient study. *Alt Ther Health Med*. 2003;9:58–62.

To the Editor:

Equivalent positive responses in both arms of their study may emphasize how little we understand about active ingredients in the injectates. Needle placement into tissue cannot be considered a placebo. More work is required for better understanding of frequency, volume, chemical composition of injectates, as well as patient selection. Unexpected are the conclusions of Dr. Loeser, which are clearly not reflective of the article itself.[1]

AQ: 3

The collected data and subsequent statistical analysis provide strong evidence of the following:

1. It is a longitudinal study, showing fairly early effect of either injection treatment (*i.e.*, saline *vs.* glucose/lignocaine), regardless of exercise status, that sustains itself over time. This is not likely the typical placebo effect one would expect to find in a longitudinal study, although longitudinal studies investigating possible placebo effects[2] have been inadequately designed to determine if a sustained placebo effect exists. Also, the observed positive sustained outcome under either injection treatment is almost surely not regression to the mean given the extended period these participants were in a suboptimal state before treatment.
2. In chronic "nonspecific" low back pain, tenderness of the connective tissue at their enthesis signifies a putative source of nociception and should be treated by injection.(3)
3. A general practitioner without extensive and prolonged training in this technique, costly radiographic equipment, auxiliary personnel, and sedation, using a modified low-risk protocol is capable of achieving immensely positive results in an office setting.(3)
4. In this study, the authors serendipitously came to a combination of volume and concentration of both injectates that produced equally beneficial results.[3] Their data support the positive outcomes of earlier randomized controlled trials on prolotherapy.[4–6] The authors also stated that the response to treatment was as good as spinal cord stimulation or multidisciplinary pain treatment.(3)

The mechanism of action of both dextrose and saline is dose related. In a solution, the dose is volume and concentration dependent. Concentration appears to be an insignificant factor in this study. However, a fairly large volume injected into connective tissue at each site may have played a significant role. Connective tissue belongs to a slow equilibrating, nonfunctional, interstitial fluid compartment[7]; thus, normal saline and dextrose remain in this compartment as an extrinsic, volume-occupying lesion for sufficient time to stimulate an inflammatory reaction.[8] Additionally, hydrostatic pressure from injection distends connective tissue fibers and traumatizes the interfascicular and extracellular matrix bonds.[8]

The trend of beneficial results after normal saline injections was visible in earlier randomized controlled trials and was presented at the 2003 annual ISIS meeting as preliminary results of the ongoing meta-analysis study.[4–6,9]

A number of different solutions have been used for "prolotherapy," including several which are overtly sclerosing. Phenol, also used in prolotherapy, has the potential advantage of being both overtly sclerosing and neurolytic, especially on small, unmyelinated C-fibers. Contemporary understanding is such that prolotherapy mechanism of action is complex and multifaceted. Cascade of inflammatory, regenerative, reparative response can be induced by: cell compression by extracellular volume, mechanical transection of cells and matrix by needle, contraction due to osmotic or chemical properties of the injectates, mediated by cytokines and multiple growth factors[10,11]:

AQ: 4

- The unexpected observations of this study herald a new day and should stimulate further work on soft tissue injection.
- Painful degenerative changes affecting connective tissue present itself both in myofascial pain syndromes and at the fibro-osseous junctions with equal intensity and frequency. Fibro-osseous injection therapy/prolotherapy deserves at least as much recognition and popularity as fibromuscular trigger point injections so vigorously advocated by Dr. Loeser.(11)
- To imply that all prolotherapy is ineffective based on one study of two new components is certainly not justified.(1)

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References

1. Loeser JD. Point of view: prolotherapy injections, saline injections, and exercises for chronic low-back pain. A randomized study. *Spine*. 2003;29:16.
2. Bouchet C, Guillemin F, Briancon S. Nonspecific effects in longitudinal studies: impact on quality of life measures. *J Clin Epidemiol*. 1996;49:15–20.
3. Yelland MJ, Glasziou PP, Bogduk N, et al. Prolotherapy injections, saline injections, and exercises for chronic low-back pain: a randomized study. *Spine*. 2003;29:9–16.
4. Dechow E, Davies RK, Carr AJ, et al. A randomized, double-blind, placebo-controlled trial of sclerosing injections in patients with chronic low back pain. *Rheumatology*. 1999;38:1255–1259.
5. Klein RG, Eek BC, DeLong WB, et al. A randomized double-blind trial of dextrose-glycerine-phenol injections for chronic, low back pain. *J Spinal Disord*. 1993;6:23–33.
6. Ongley MJ, Klein RG, Dorman TA, et al. A new approach to the treatment of chronic low back pain. *Lancet*. 1987;2:143–146.
7. Schwartz SI, Shires GT, Spencer FC, et al. *Principals of Surgery*, 7ed ed. New York: McGraw-Hill, 1999.
8. Cotran RS, et al. *Robbins Pathological Basis of Disease*. Philadelphia: Saunders, 1999.
9. Linetsky FS, Derby R, Saberski L, et al. Regenerative injection therapy/prolotherapy: a literature review with meta-analysis, a work in progress. *ISIS 11th Annual Scientific Meeting*, Orlando, FL, August 8–10, 2003.
10. Linetsky FS, Miguel R, Saberski L. Pain management with regenerative injection therapy (RIT). In: Weiner RS, ed. *Pain Management: A Practical Guide for Clinicians*. Washington, DC: American Academy of Pain Management, 381–401.
11. Sola AE, Bonica JJ. Myofascial pain syndromes. In: Loeser JD, ed. *Bonica's Management of Pain*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2001.

AQ: 5

To the Editor:

With regard to the Yelland *et al* paper, the most significant conclusion appears to be that needling ligaments gives lasting relief to patients with all sorts of relatively undiagnosed low back pain. This is interesting in its own right but says little about prolotherapy, which is presumably the primary object of the study.

The authors state that, "Prolotherapy is a treatment for chronic nonspecific low back pain." I believe very few physicians using prolotherapy would agree with this. Prolotherapy is not a treatment for pain, but rather for specific structural weakness, often referred to as "ligament laxity." In other words, it is directed at abnormal mechanics, not at the experience of pain.

The difficulty arises in diagnosing ligament laxity. There are different schools of thought about this. At one extreme is the Hackett school, which identifies lax ligaments simply by tenderness on palpation. Presumably, the authors were most influenced by this method. However, even here diagnosis should be confirmed by reproduction of the pain of complaint and subsequent relief by injection of local anesthesia.[1] Other schools of thought look for evidence of joint instability by history[2] and/or by physical examination.[3,4] Depending on the school of thought, varying proportions of "chronic nonspecific low back pain" fulfill these criteria.

The concept of nonspecific low back pain is in any case anachronistic. There is no shortage of literature (osteopathic, chiropractic, and medical) describing multiple potential causes of low back pain. To ignore this is to defeat any effort at treating low back pain, by prolotherapy or any other method.

Treating chronic nonspecific low back pain with prolotherapy is analogous to treating nonspecific abdominal pain by appendectomy. Both are useful treatments, but the treatment can be no better than the diagnosis.

Robert Kidd, MD, CM
Renfrew, Ontario, Canada AQ: 6

References

1. Hackett GH, Hemwall GA, Montgomery GA. *Ligament and Tendon Relaxation Treated by Prolotherapy*, 5th ed. Oak Park, IL: Gustav A. Hemwall, 1991.
2. Barbor R. Sclerosant therapy, the theory of treatment of ligamentous disturbance by a dextrose sclerosant. *Reunion Sobre Patologia de la Columina Vertebral*. Murcia, Spain. March 30, 1977.
3. Gedney EH. Hypermobile joint: a preliminary report. *Osteopath Prof*. 1937; 4:30–31.
4. Gedney EH. Disk syndrome, new approach in the treatment of symptomatic intervertebral disk. *Osteopath Prof*. 1951;18:12:11–46.

In Response:

Several important issues have been raised in the letters to the editor about our trial of prolotherapy for chronic low back pain: the positive results shown by both injection groups, the choice of control group, limitations of the injection technique used, and the appropriateness of patient selection.

In one respect, the results of this study vindicate the use of prolotherapy in that it showed sustained and significant results at 2 years, four times longer than the follow-up in the previous three studies in this area.[1–3] It showed similar efficacy to spinal fusion, but at a much lower cost.[4] However, because of the similar response of prolotherapy injections to control injections of saline, the study will be regarded by skeptics as evidence that prolotherapy does not work. This interpretation may, in part, be a consequence of the central aim of the study, namely, to assess the effect of the glucose and lignocaine in the injection solution, rather than the effect of the whole prolotherapy protocol. Consequently, we chose isotonic saline injections for the control group. This treatment is often incorrectly labeled as a placebo, ignoring the possible effects of other components of the injections, including the trauma of the needles, the stretching of ligaments by large volumes of fluid and the skin wheals of lignocaine over the injection sites and, of course, the physician administering the injections. These were applied equally to each group. Testing these other components of treatment requires a different control, such as the superficial injections suggested by Reeves et al. Such a control was seriously considered for our study, but a saline group was preferred because of the importance placed by prolotherapists on the composition of the injection solution.

The letters commenting on our trial echo a concern commonly raised about acupuncture trials, namely, the lack of consensus about treatment protocols. Our trial was designed to test the prolotherapy protocol popularized in Australia by Dhillon.[5] This protocol can be safely

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performed in primary care setting without sedation. It involves fewer injections than some protocols by targeting only tender ligaments and entheses, consistent with the distribution of the pain. At each puncture site, a number of points are injected, resulting in an average of 20 points, compared with 30 to 40 points in protocols in the early trials.[1,2] Treatment of the deep sacroiliac ligaments is restricted to slow responders. Despite differences in protocols, our saline controls responded as well as those in the original trial of prolotherapy for chronic low back pain.[1] This raises doubts about the need to treat nontender points and leads to the next issue of the composition and osmolarity of the injection solution. In the first two trials,[1,2] superior results were achieved at 6 months with the glucose-glycerin-phenol-lignocaine solution, but the attributable effect was clouded by cointerventions, including manipulation. In the third trial, this solution showed no effect when used in small volumes on only three occasions with no cointerventions.[3]

The methods of patient selection were modeled on those used in all previous trials of prolotherapy for chronic low back pain, to allow comparability of results. They are in keeping with those recommended by the founder of modern-day prolotherapy, George Hackett.[6] In essence, prolotherapists treat patients with pain of mechanical origin, where an assumption is made that the pain is of ligamentous or tenoperiosteal origin. Injection sites are guided by the presence of tenderness in ligaments and entheses consistent with the distribution of the pain. Patient selection based on clinical features of instability lends itself to criticism as there are no validated criteria for the diagnosis of instability.

Our trial should not be the final word on prolotherapy. The next priority for trials on prolotherapy is a direct comparison with a common noninjection treatment applied with similar enthusiasm. This will give insights into the effect of repeated injections and better define the place of prolotherapy in the vast selection of treatments for chronic low back pain.

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References

1. Ongley MJ, Klein RG, Dorman TA, et al. A new approach to the treatment of chronic low back pain. *Lancet*. 1987;2:143–146.
2. Klein RG, Eek BC, DeLong WB, et al. A randomized double-blind trial of dextrose-glycerine-phenol injections for chronic, low back pain. *J Spinal Disord*. 1993;6:23–33.
3. Dechow E, Davies RK, Carr AJ, et al. A randomized, double-blind, placebo-controlled trial of sclerosing injections in patients with chronic low back pain. *Rheumatology*. 1999;38:1255–1259.
4. Fritzell P, Hagg O, Wessberg P, et al. 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. *Spine*. 2001;26:2521–2532.
5. Dhillon GS. Prolotherapy in lumbo-pelvic pain. *Aust Musculoskeletal Med*. 1997;2:17–19.
6. Hackett GS, Hemwall GA, Montgomery GA. *Ligament and Tendon Relaxation Treated by Prolotherapy*, 5th ed. Oak Park, IL: Gustav A. Hemwall, 1993:14–15.

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