



PASIG PERFORMING ARTS

SPECIAL INTEREST GROUP



PASIG MONTHLY CITATION BLAST: No.39

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Dear PASIG members:

In these challenging economic times, many of our performing arts organizations are stressed to the maximum. Some symphony and ballet companies have already closed and it is likely that more will not survive. As performing arts clinicians, we can roll up our sleeves and pitch in by holding the line on physical therapy costs and giving back when we can. Our society needs art. Art is a powerful means of presenting truths about humankind that cannot be expressed any other way. It connects us.

For this March Citation BLAST, I've selected a topic that periodically I'm asked about: *Prolotherapy*. The format is an annotated bibliography of articles on the selected topic from 1998 – 2008. Anyone interested in contributing a special topic citation blast, please volunteer. The BLASTS and updated libraries are posted on the PASIG webpage for our members to access and download. (Information about EndNote referencing software can be found at <http://www.endnote.com>, including a 30-day free trial).

As always, your comments and suggestions are welcome. Please drop me an e-mail anytime.

Regards,
Shaw

Shaw Bronner PT, PhD, OCS
Chair, PASIG Research Committee
sbronner@liu.edu

Prolotherapy

Periodically we're asked about *prolotherapy* by a dancer who is desperate to be well and avoiding more invasive intervention. It's a difficult answer as the literature is limited

with respect to randomized clinical trials and systematic reviews are mixed with respect to treatment efficacy.

Prolotherapy is an alternative therapy for chronic musculoskeletal injury including joint laxity. Most commonly, a dextrose sclerosing solution is used which may contain lidocaine as well. Post-injection inflammation, pain, and stiffness are frequently reported. The mechanical effects of prolotherapy injections compared to saline and no treatment following induced ligament stretch injury were investigated with rats (Jensen et al., 2008). While the prolotherapy group ligaments were found to have increased cross-sectional areas, there were no differences between groups in laxity or mechanical properties, and no change in collagen fibril density or diameter. Therefore it is unclear what effect prolotherapy has on tissue in the long-term.

Shaw Bronner PT, PhD, OCS
ADAM Center, Long Island University

Centeno CJ, Elliott J, et al. (2005). Fluoroscopically guided cervical prolotherapy for instability with blinded pre and post radiographic reading. Pain Physician 8(1): 67-72.

BACKGROUND: Several authors have postulated that cervical instability is a major cause of traumatic spinal pain. OBJECTIVE: The purpose of this prospective case series study (n = 6) was to determine if proliferant injections have an effect on cervical translation as measured by a blinded reader. DESIGN: This study was a prospective case series. Study participants were selected from patients seen for the primary complaint of Motor Vehicle Collision related neck pain in a private sub-specialty pain clinic. METHODS: Flexion and extension views were obtained by standard radiographs taken with a C-Arm fluoroscope under Valium sedation. Patients with more than 2.7 mm of absolute cervical translation and at least 50% reduction of cervical and referred pain with a two day rigid cervical immobilization test were admitted into the study. Participants underwent 3 prolotherapy injections at all sites that demonstrated translation. The difference in means between pre-test and post-test measurements (flexion translation, extension translation, and pain VAS scores) were assessed by a Wilcoxon signed ranks test (alpha = 0.05). RESULTS: The mean post-test VAS score (M= 3.83, SD=2.3, t=2.889) was significantly less (p=0.04) than the mean pre-test VAS score (M=5.75, SD=1.94). The correlation between difference in mean extension at C2-3 and C5-6 and difference in mean extension was significant (rho=0.89, p=0.02 and rho=0.85, p=0.03 respectively). Difference in mean flexion at C3-4 and C4-5 was significantly correlated with difference in mean flexion (rho=0.88, p=0.02 and rho=0.941, p <0.01 respectively). CONCLUSIONS: The results of this study demonstrate statistically significant correlations between proliferant injections, a reduction of both cervical flexion and extension translation, as well as a reduction in pain VAS score. Since patients with traumatic cervical instability have few viable treatment options other than surgical fusion, cervical proliferant injections under C-Arm fluoroscope may be a viable treatment option.

Centeno CJ, Schultz J, et al. (2008). Sclerotherapy of Baker's cyst with imaging confirmation of resolution. Pain Physician 11(2): 257-61.

BACKGROUND: Baker's cysts are commonly encountered in pain management practices. OBJECTIVE: To ascertain if sclerotherapy treatment of a Baker's cyst could produce

objectively verifiable MRI imaging changes. DESIGN: Case report. METHODS: A 52-year-old white male with a posterior horn of the medial meniscus tear and a large Baker's cyst who had failed conservative care and drainage was imaged before treatment with sclerosing. Three injections of 12.5% dextrose and anesthetic with sodium morrhuate were injected intraarticular into the right knee after drainage. RESULTS: The Baker's cyst resolved on both postoperative imaging after the completion of care as well as on physical examination. CONCLUSIONS: Prolotherapy in this case study seemed to be an effective treatment for Baker's cyst in this patient.

Chakraverty R, Dias R (2004). Audit of conservative management of chronic low back pain in a secondary care setting--part I: facet joint and sacroiliac joint interventions. Acupunct Med **22**(4): 207-13.

The work of a chronic back pain service in secondary care in the West Midlands is reported. The service offers acupuncture, spinal injection procedures, osteopathy and a range of other interventions for patients whose back pain has not responded to conservative management. This section of the report focuses on injection procedures for lumbar facet joint and sacroiliac joint pain, which have been shown to be the cause of chronic low back pain in 16-40% and 13-19% of patients respectively. Diagnosis relies on the use of intra-articular or sensory nerve block injections with local anaesthetic. Possible treatments following diagnosis include intra-articular corticosteroid, radiofrequency denervation (for facet joint pain) or ligament prolotherapy injections (for sacroiliac joint pain). The results of several hospital audits are reported. At six month follow up, 50% of 38 patients undergoing radiofrequency denervation following diagnostic blocks for facet joint pain had improved by more than 50%, compared to 29% of 34 patients treated with intra-articular corticosteroid injection. Sixty three per cent of 19 patients undergoing prolotherapy following diagnostic block injection for sacroiliac joint pain had improved at six months, compared to 33% of 33 who had intra-articular corticosteroid. Both radiofrequency denervation and sacroiliac prolotherapy showed good long-term outcomes at one year.

Choi H, McCartney M, et al. (2008). Treatment of Osteitis Pubis and Osteomyelitis of the Pubic Symphysis in Athletes: A Systematic Review. Br J Sports Med.

OBJECTIVES: We examined the most current evidence for treatment options in athletes with osteitis pubis and osteomyelitis pubis, attempting to determine which options provide optimal pain relief with rapid return to sport and prevention of symptom reoccurrence. METHODS: Three databases-MEDLINE, Cochrane Database of Systematic Reviews and CINAHL were searched using the OVID interface for all years between 1985 and May 2008. References were analyzed from included studies and additional relevant articles were obtained for inclusion. Inclusion criteria included: 1) humans only, (2) subjects had no apparent risk factors for development of osteitis pubis or osteomyelitis of the pubic symphysis other than athletic involvement, (3) both physical exam findings and diagnostic imaging were used to confirm either diagnosis, and (4) a definitive treatment strategy was identifiable for management of osteitis pubis or osteomyelitis of the pubic symphysis. In total, 25 articles were included in the review. RESULTS: There were no randomized controlled trials (RCTs) identified with our search strategy. 195 athletes were diagnosed with osteitis pubis (186 males, 9 females) and treated with either conservative measures/physical therapy, local injection with corticosteroids and/or local anesthetic, dextrose prolotherapy, surgery or antibiotic therapy. Six case reports/series described conservative treatment measures (physical therapy, rest, NSAIDs). Four case series explored the use of corticosteroid injections in treatment. One case series described the use of dextrose prolotherapy as a treatment modality. Six case series described various surgical techniques (pubic symphysis curettage, polypropylene mesh placement, and pubic bone stabilization) in

treatment. Ten case reports/series (10 subjects) outlined antibiotic treatment of osteomyelitis of the pubic symphysis. CONCLUSIONS: The current medical literature shows only level 4 evidence for the treatment of osteitis pubis in twenty-four case reports/series in athletes. Without any direct comparison of treatment modalities it is difficult to determine which individual treatment option is the most efficacious. Further study comparing the different treatment options is necessary to determine which modality provides the fastest return to sport.

Chou R, Atlas J, et al. (2009). Nonsurgical Interventional Therapies for Low Back Pain: A Review of the Evidence for an American Pain Society Clinical Practice Guideline. *Spine*.
STUDY DESIGN: Systematic review. OBJECTIVE: To systematically assess benefits and harms of nonsurgical interventional therapies for low back and radicular pain. SUMMARY OF BACKGROUND DATA: Although use of certain interventional therapies is common or increasing, there is also uncertainty or controversy about their efficacy. METHODS: Electronic database searches on Ovid MEDLINE and the Cochrane databases were conducted through July 2008 to identify randomized controlled trials and systematic reviews of local injections, botulinum toxin injection, prolotherapy, epidural steroid injection, facet joint injection, therapeutic medial branch block, sacroiliac joint injection, intradiscal steroid injection, chemonucleolysis, radiofrequency denervation, intradiscal electrothermal therapy, percutaneous intradiscal radiofrequency thermocoagulation, Coblation nucleoplasty, and spinal cord stimulation. All relevant studies were methodologically assessed by 2 independent reviewers using criteria developed by the Cochrane Back Review Group (for trials) and by Oxman (for systematic reviews). A qualitative synthesis of results was performed using methods adapted from the US Preventive Services Task Force. RESULTS: For sciatica or prolapsed lumbar disc with radiculopathy, we found good evidence that chemonucleolysis is moderately superior to placebo injection but inferior to surgery, and fair evidence that epidural steroid injection is moderately effective for short-term (but not long-term) symptom relief. We found fair evidence that spinal cord stimulation is moderately effective for failed back surgery syndrome with persistent radiculopathy, though device-related complications are common. We found good or fair evidence that prolotherapy, facet joint injection, intradiscal steroid injection, and percutaneous intradiscal radiofrequency thermocoagulation are not effective. Insufficient evidence exists to reliably evaluate other interventional therapies. CONCLUSION: Few nonsurgical interventional therapies for low back pain have been shown to be effective in randomized, placebo-controlled trials.

Dagenais S, Haldeman S, et al. (2005). Intraligamentous injection of sclerosing solutions (prolotherapy) for spinal pain: a critical review of the literature. *Spine J* 5(3): 310-28.
BACKGROUND CONTEXT: The injection of various solutions aimed at producing a sclerosing effect has been used to treat soft tissues injuries (eg, inguinal hernia) for more than 100 years. In the 1930s, this treatment approach was applied to injured joints in an attempt to stimulate connective tissue repair. Although several studies have been published about this method of treatment for various orthopedic and spinal indications (termed prolotherapy), its use remains controversial. PURPOSE: To conduct a critical review of the literature on prolotherapy for spinal pain. STUDY DESIGN/SETTING: Critical review of the literature. METHODS: Computerized medical literature databases (Medline, CINAHL, Mantis, Cochrane Central Register of Controlled Trials) were searched to uncover all published information about the use of sclerosing injections in humans with spinal pain disorders. Search results were reviewed for relevance, and information was abstracted from full-text articles. RESULTS: Our search uncovered almost 200 reference materials in various media related to prolotherapy, including 31 clinical studies related to spinal pain. There were 26 observational cohorts and 5 randomized clinical trials (RCTs). Indications in these studies

were low back pain (22), neck pain (3), cervical headaches (3) and dorsal or thoracic pain (3). A total of 20 sclerosing solutions were used in these studies; the most common was a mixture of dextrose 12.5%, glycerin 12.5%, phenol 1.25% and lidocaine 0.25%. Wide variations were found in treatment protocols, such as dose, number of treatments and use of adjunct therapies. Most cohort studies were only of moderate quality and varied greatly in the substances injected and the use of co-interventions. Most clinical studies reported positive results such as decreased pain or disability, although differences between treatment and control groups did not always reach statistical significance. Commonly reported adverse reactions to this treatment include temporary postinjection pain and stiffness. A handful of more serious adverse events were reported in the 1950s and 1960s with stronger or unknown solutions. CONCLUSION: Prolotherapy describes a variety of treatment approaches rather than a specific protocol. Results from clinical studies published to date indicate that it may be effective at reducing spinal pain. Great variation was found in the injection and treatment protocols used in these studies that preclude definite conclusions. Future research should focus on those solutions and protocols that are most commonly used in clinical practice and have been used in trials reporting effectiveness to help determine which patients, if any, are most likely to benefit from this treatment.

Dagenais S, Ogunseitan O, et al. (2006). Side effects and adverse events related to intraligamentous injection of sclerosing solutions (prolotherapy) for back and neck pain: A survey of practitioners. *Arch Phys Med Rehabil* **87**(7): 909-13.

OBJECTIVE: To study the side effects and adverse events related to intraligamentous injection of sclerosing solutions (prolotherapy) for back and neck pain. DESIGN: Practitioner postal survey. SETTING: Postal survey of practitioners of prolotherapy for back and neck pain in the United States and Canada. PARTICIPANTS: A sample of prolotherapy practitioners from 2 professional organizations were surveyed about their training and experience, use of specific treatment procedures, estimated prevalence of side effects, and adverse events related to prolotherapy for back and neck pain. INTERVENTIONS: Not applicable. MAIN OUTCOME MEASURES: Prevalence of side effects and adverse events. RESULTS: Surveys were completed by 171 practitioners (response rate, 50%). Ninety-eight percent held medical degrees, and 83% were board certified in various disciplines. Respondents had a median of 10 years of experience, during which they had treated a median of 500 patients and given a median of 2000 treatments. Side effects with the highest median estimated prevalence were pain (70%), stiffness (25%), and bruising (5%). There were 472 reports of adverse events, including 69 that required hospitalization and 5 that resulted in permanent injury secondary to nerve injury. The vast majority (80%) were related to needle injuries such as spinal headache (n = 164), pneumothorax (n=123), temporary systemic reactions (n = 73), nerve damage (n = 54), hemorrhage (n = 27), nonsevere spinal cord insult (ie, meningitis, paralysis, spinal cord injury) (n = 9), and disk injury (n = 2). CONCLUSIONS: Side effects related to prolotherapy for back and neck pain, such as temporary postinjection pain, stiffness, and bruising, are common and benign. Adverse events related to prolotherapy for back and neck pain are similar in nature to other widely used spinal injection procedures. Further study is needed to fully describe the adverse event profile of prolotherapy for back and neck pain.

Dagenais S, Yelland MJ, et al. (2007). Prolotherapy injections for chronic low-back pain. *Cochrane Database Syst Rev*(2): CD004059.

BACKGROUND: Prolotherapy involves repeated injections of irritant solutions to strengthen lumbosacral ligaments and reduce some types of chronic low-back pain; spinal manipulation and exercises are often used to enhance its effectiveness. OBJECTIVES: To determine the efficacy of prolotherapy in adults with chronic low-back pain. SEARCH STRATEGY: We

searched CENTRAL 2006, Issue 3 and MEDLINE, EMBASE, CINAHL, and AMED from their respective beginnings to October 2006, with no restrictions on language, and consulted content experts. **SELECTION CRITERIA:** We included randomised (RCT) and quasi-randomised controlled trials (QRCT) that compared prolotherapy injections to control injections, alone or in combination with other treatments, which measured pain or disability before and after the intervention. **DATA COLLECTION AND ANALYSIS:** Two review authors independently selected the trials and assessed methodological quality. Intervention protocols varied from study to study, making meta-analysis impossible. **MAIN RESULTS:** We identified five high quality studies with a total of 366 participants. All measured pain or disability levels at six months, and four measured the proportion of participants reporting a greater than 50% reduction in pain or disability scores. Three randomized controlled trials (206 participants) found that prolotherapy injections alone are no more effective than control injection for chronic low-back pain and disability. At six months, there was no difference between groups in mean pain or disability scores (2 RCTs; 184 participants) and no difference in proportions who reported over 50% improvement in pain or disability (3 RCTs; 206 participants). These trials could not be pooled due to clinical heterogeneity. Two RCTs (160 participants) found that prolotherapy injections, given with spinal manipulation, exercise, and other therapies, are more effective than control injections for chronic low-back pain and disability. At six months, one study reported a significant difference between groups in mean pain and disability scores, whereas the other study did not. Both studies reported a significant difference in the proportion of individuals who reported over 50% reduction in disability or pain. Co-interventions confounded interpretation of results and clinical heterogeneity in the trials prevented pooling. **AUTHORS' CONCLUSIONS:** There is conflicting evidence regarding the efficacy of prolotherapy injections for patients with chronic low-back pain. When used alone, prolotherapy is not an effective treatment for chronic low-back pain. When combined with spinal manipulation, exercise, and other co-interventions, prolotherapy may improve chronic low-back pain and disability. Conclusions are confounded by clinical heterogeneity amongst studies and by the presence of co-interventions.

Forst SL, Wheeler MT, et al. (2006). The sacroiliac joint: anatomy, physiology and clinical significance. *Pain Physician* 9(1): 61-7.

The sacroiliac joint (SIJ) is a putative source of low back pain. The objective of this article is to provide clinicians with a concise review of SIJ structure and function, diagnostic indicators of SIJ-mediated pain, and therapeutic considerations. The SIJ is a true diarthrodial joint with unique characteristics not typically found in other diarthrodial joints. The joint differs with others in that it has fibrocartilage in addition to hyaline cartilage, there is discontinuity of the posterior capsule, and articular surfaces have many ridges and depressions. The sacroiliac joint is well innervated. Histological analysis of the sacroiliac joint has verified the presence of nerve fibers within the joint capsule and adjoining ligaments. It has been variously described that the sacroiliac joint receives its innervation from the ventral rami of L4 and L5, the superior gluteal nerve, and the dorsal rami of L5, S1, and S2, or that it is almost exclusively derived from the sacral dorsal rami. Even though the sacroiliac joint is a known putative source of low back and lower extremity pain, there are few findings that are pathognomonic of sacroiliac joint pain. The controlled diagnostic blocks utilizing the International Association for the Study of Pain (IASP) criteria demonstrated the prevalence of pain of sacroiliac joint origin in 19% to 30% of the patients suspected to have sacroiliac joint pain. Conservative management includes manual medicine techniques, pelvic stabilization exercises to allow dynamic postural control, and muscle balancing of the trunk and lower extremities. Interventional treatments include sacroiliac joint, intra-articular joint injections, radiofrequency neurotomy, prolotherapy, cryotherapy, and surgical treatment.

The evidence for intra-articular injections and radiofrequency neurotomy has been shown to be limited in managing sacroiliac joint pain.

Hakala RV (2005). Prolotherapy (proliferation therapy) in the treatment of TMD. Cranio **23**(4): 283-8.

Proliferation therapy, or "prolotherapy," is also known as regenerative injection therapy (RIT). Since the 1930s, the technique has been used to stabilize injured joints and to relieve joint pain. This article reviews the history and scientific literature regarding prolotherapy and describes the application of the technique to treat injured or unstable temporomandibular joints (TMJ). Alternative medicaments and the likely mechanisms of action are discussed. A brief preliminary summary of a retrospective clinical study of the efficacy of prolotherapy is included. The study shows that prolotherapy can be an effective therapeutic modality that reduces TMJ pain and joint noise in a majority of patients who have reached a plateau with use of an intraoral appliance, physical therapy, and home care.

Jansen JA, Mens JM, et al. (2008). Treatment of longstanding groin pain in athletes: a systematic review. Scand J Med Sci Sports **18**(3): 263-74.

The aims of this study were to determine (1) the kinds of treatments applied for longstanding groin pain (LGP) in athletes; (2) the results; and (3) the levels of evidence for the interventions. Digital databases P were searched for articles describing the effects of interventions for LGP in athletes. Treatment of LGP in athletes can consist of conservative measures such as rest or restricted activity, active or passive physical therapy, steroid injections or dextrose prolotherapy. Studies describing surgery generally mention failure of conservative measures, although a description of these conservative measures is mostly lacking. During surgery, a reinforcement of the abdominal wall is applied in most cases, using an open or laparoscopic approach. There is level I evidence that physical therapy aiming at strengthening and coordinating the muscles stabilizing hip and pelvis has superior results compared with passive physical therapy. For patients with a positive herniography and/or positive ilioinguinal or iliohypogastric nerve block tests, there are indications (level II) that surgery results in earlier return to sport compared with exercise therapy. Possibly, laparoscopic intervention might result in an earlier return to sport compared with open approach surgery (level III). For different clinical diagnoses, the same or similar surgical interventions were performed.

Jensen KT, Rabago DP, et al. (2008). Early inflammatory response of knee ligaments to prolotherapy in a rat model. J Orthop Res **26**(6): 816-23.

Prolotherapy is an alternative injection-based therapy for chronic musculoskeletal pain. Three different proliferants, D-glucose (dextrose), phenol-glucose-glycerine (P2G), and sodium morrhuate, used in prolotherapy are hypothesized to strengthen and reorganize chronically injured soft tissue and decrease pain through modulation of the inflammatory process. Our hypothesis is that commonly used prolotherapy solutions will induce inflammation (leukocyte and macrophage infiltration) in medial collateral ligaments (MCLs) compared to needlestick, saline injection, and no-injection controls. MCLs of 84 Sprague-Dawley rats were injected one time at both the tibial and femoral insertions. Immunohistochemistry (IHC) was used to determine the inflammatory response at three locations (tibial and femoral insertions and midsubstance) 6, 24, and 72 h after dextrose injection compared to saline- and no-injection controls and collagenase (positive control) (n = 4). qPCR was used to analyze gene expression 24 h postinjection (n = 4). Sodium morrhuate, P2G, and needlestick control were also investigated after 24 h (n = 4). In general, inflammation (CD43+, ED1+, and ED2+ cells) increased after prolotherapy injection compared to no-injection control but did not increase consistently compared to saline and

needlestick control injections. This response varied by both location and proliferant. Inflammation was observed at 6 and 24 h postinjection but was resolved by 72 h compared to no-injection controls ($p < 0.05$). CD43+ leukocytes and ED2+ macrophages increased compared to needlestick and saline-injection control, respectively, 24 h postinjection ($p < 0.05$). Prolotherapy injections created an inflammatory response, but this response was variable and overall, not uniformly different from that caused by saline injections or needlestick procedures.

Jensen KT, Rabago DP, et al. (2008). Response of knee ligaments to prolotherapy in a rat injury model. *Am J Sports Med* **36**(7): 1347-57.

BACKGROUND: Prolotherapy is an alternative therapy for chronic musculoskeletal injury including joint laxity. The commonly used injectant, D-glucose (dextrose), is hypothesized to improve ligament mechanics and decrease pain through an inflammatory mechanism. No study has investigated the mechanical effects of prolotherapy on stretch-injured ligaments. **HYPOTHESES:** Dextrose injections will enlarge cross-sectional area, decrease laxity, strengthen, and stiffen stretch-injured medial collateral ligaments (MCLs) compared with controls. Dextrose prolotherapy will increase collagen fibril diameter and density of stretch-injured MCLs. **STUDY DESIGN:** Controlled laboratory study. **METHODS:** Twenty-four rats were bilaterally MCL stretch-injured, and the induced laxity was measured. After 2 weeks, 32 MCLs were injected twice, 1 week apart, with either dextrose or saline control; 16 MCLs received no injection. Seven uninjured rats (14 MCLs) were additional controls. Two weeks after the second injection, ligament laxity, mechanical properties ($n = 8$), and collagen fibril diameter and density ($n = 3$) were assessed. **RESULTS:** The injury model created consistent ligament laxity ($P < .05$) that was not altered by dextrose injections. Cross-sectional area of dextrose-injected MCLs was increased 30% and 90% compared with saline and uninjured controls, respectively ($P < .05$). Collagen fibril diameter and density were decreased in injured ligaments compared with uninjured controls ($P < .05$), but collagen fibril characteristics were not different between injured groups. **CONCLUSION:** Dextrose injections increased the cross-sectional area of MCLs compared with saline-injected and uninjured controls. Dextrose injections did not alter other measured properties in this model. **CLINICAL RELEVANCE:** Our results suggest that clinical improvement from prolotherapy may not result from direct effects on ligament biomechanics.

Khan SA, Kumar A, et al. (2008). Dextrose prolotherapy for recalcitrant coccygodynia. *J Orthop Surg (Hong Kong)* **16**(1): 27-9.

PURPOSE: To present the results of dextrose prolotherapy undertaken for chronic non-responding coccygodynia in 37 patients. **METHODS:** 14 men and 23 women (mean age, 36 years) with chronic coccygodynia not responding to conservative treatment for more than 6 months were included. 27 of them had received local steroid injections. A visual analogue score (VAS) was recorded for all patients before and after injection of 8 ml of 25% dextrose and 2 ml of 2% lignocaine into the coccyx. In 8 patients with a VAS of more than 4 after the second injection, a third injection was given 4 weeks later. **RESULTS:** The mean VAS before prolotherapy was 8.5. It was 3.4 after the first injection and 2.5 after the second injection. Minimal or no improvement was noted in 7 patients; the remaining 30 patients had good pain relief. **CONCLUSION:** Dextrose prolotherapy is an effective treatment option in patients with chronic, recalcitrant coccygodynia and should be used before undergoing coccygectomy. Randomised studies are needed to compare prolotherapy with local steroid injections or coccygectomies.

Kim SR, Stitik TP, et al. (2004). Critical review of prolotherapy for osteoarthritis, low back pain, and other musculoskeletal conditions: a physiatric perspective. Am J Phys Med Rehabil **83**(5): 379-89.

The current scientific literature relevant to the use of prolotherapy for osteoarthritis, low back pain, and other musculoskeletal conditions was reviewed and critically analyzed to determine a clinical effect. Three randomized, controlled studies were found studying the use of dextrose/glycerine/phenol prolotherapy for chronic low back pain; however, they were inconclusive due to the lack of adequate controls, heterogeneity in patient diagnoses, and variations in solutions injected. Two randomized, controlled studies were found that provide some evidence supporting the use of 10% dextrose prolotherapy for osteoarthritis. The sample size of the study (n = 13) involving osteoarthritic thumbs and fingers may have been too small to be strongly conclusive; however, it provides preliminary data to support future studies. Two studies involving osteoarthritic knees report an improvement in anterior cruciate ligament laxity; however, they did not have control groups for comparison. Only case reports were found supporting the pursuit of controlled clinical studies of prolotherapy for chronic neck pain. On the basis of the scarce body of literature critically reviewed to date, the clinical efficacy of prolotherapy in treating osteoarthritis, low back pain, and other musculoskeletal conditions remains inconclusive.

Rabago D, Best TM, et al. (2005). A systematic review of prolotherapy for chronic musculoskeletal pain. Clin J Sport Med **15**(5): 376-80.

OBJECTIVE: Prolotherapy, an injection-based treatment of chronic musculoskeletal pain, has grown in popularity and has received significant recent attention. The objective of this review is to determine the effectiveness of prolotherapy for treatment of chronic musculoskeletal pain. **DATA SOURCES:** We searched Medline, PreMedline, Embase, CINAHL, and Allied and Complementary Medicine with search strategies using all current and historical names for prolotherapy and injectants. Reference sections of included articles were scanned, and content area specialists were consulted. **STUDY SELECTION:** All published studies involving human subjects and assessing prolotherapy were included. **MAIN RESULTS:** Data from 34 case reports and case series and 2 nonrandomized controlled trials suggest prolotherapy is efficacious for many musculoskeletal conditions. However, results from 6 randomized controlled trials (RCTs) are conflicting. Two RCTs on osteoarthritis reported decreased pain, increased range of motion, and increased patellofemoral cartilage thickness after prolotherapy. Two RCTs on low back pain reported significant improvements in pain and disability compared with control subjects, whereas 2 did not. All studies had significant methodological limitations. **CONCLUSIONS:** There are limited high-quality data supporting the use of prolotherapy in the treatment of musculoskeletal pain or sport-related soft tissue injuries. Positive results compared with controls have been reported in nonrandomized and randomized controlled trials. Further investigation with high-quality randomized controlled trials with noninjection control arms in studies specific to sport-related and musculoskeletal conditions is necessary to determine the efficacy of prolotherapy.

Rabago D, Best TM, et al. (2009). A systematic review of four injection therapies for lateral epicondylitis: prolotherapy, polidocanol, whole blood and platelet rich plasma. Br J Sports Med.

OBJECTIVE: To appraise existing evidence for prolotherapy, polidocanol, autologous whole blood and platelet-rich plasma injection therapies for lateral epicondylitis (LE). **DESIGN:** Systematic Review. **DATA SOURCES:** Medline, Embase, CINAHL, Cochrane Central Register of Controlled Trials, Allied and Complementary Medicine. **Search strategy:** names and descriptors of the therapies and LE. **Study Selection:** All human studies assessing the four therapies for LE. **MAIN RESULTS:** Results of five prospective case series and four

controlled trials (3 prolotherapy, 2 polidocanol, 3 autologous whole blood and 1 platelet-rich plasma) suggest each of the four therapies is effective for LE. In follow-up periods ranging from 9 to 108 weeks, studies reported sustained, statistically significant ($p < 0.05$) improvement on visual analog scale primary outcome pain score measures and disease specific questionnaires; relative effect sizes ranged from 51% to 94%; Cohen's d ranged from 0.68 to 6.68. Secondary outcomes also improved, including biomechanical elbow function assessment (polidocanol and prolotherapy), presence of abnormalities and increased vascularity on ultrasound (autologous whole blood and polidocanol). Subjects reported satisfaction with therapies on single-item assessments. All studies were limited by small sample size. CONCLUSIONS: There is strong pilot-level evidence supporting the use of prolotherapy, polidocanol, autologous whole blood and platelet-rich plasma injections in the treatment of LE. Rigorous studies of sufficient sample size, assessing these injection therapies using validated clinical, radiological and biomechanical measures, and tissue injury/healing-responsive biomarkers, are needed to determine long-term effectiveness and safety, and whether these techniques can play a definitive role in the management of LE and other tendinopathies.

Reeves KD, Hassanein K (2000). Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. Altern Ther Health Med 6(2): 68-74, 77-80.

CONTEXT: Use of prolotherapy (injection of growth factors or growth factor stimulators). OBJECTIVE: Determine the effects of dextrose prolotherapy on knee osteoarthritis with or without anterior cruciate ligament (ACL) laxity. DESIGN: Prospective randomized double-blind placebo-controlled trial. SETTING: Outpatient physical medicine clinic. PATIENTS OR OTHER PARTICIPANTS: Six months or more of pain along with either grade 2 or more joint narrowing or grade 2 or more osteophytic change in any knee compartment. A total of 38 knees were completely void of cartilage radiographically in at least 1 compartment. INTERVENTION: Three bimonthly injections of 9 cc of either 10% dextrose and .075% lidocaine in bacteriostatic water (active solution) versus an identical control solution absent 10% dextrose. The dextrose-treated joints then received 3 further bimonthly injections of 10% dextrose in open-label fashion. MAIN OUTCOME MEASURES: Visual analogue scale for pain and swelling, frequency of leg buckling, goniometrically measured flexion, radiographic measures of joint narrowing and osteophytosis, and KT1000-measured anterior displacement difference (ADD). RESULTS: All knees: Hotelling multivariate analysis of paired observations between 0 and 6 months for pain, swelling, buckling episodes, and knee flexion range revealed significantly more benefit from the dextrose injection ($P = .015$). By 12 months (6 injections) the dextrose-treated knees improved in pain (44% decrease), swelling complaints (63% decrease), knee buckling frequency (85% decrease), and in flexion range (14 degree increase). Analysis of blinded radiographic readings of 0- and 12-month films revealed stability of all radiographic variables except for 2 variables which improved with statistical significance. (Lateral patellofemoral cartilage thickness [$P = .019$] and distal femur width in mm [$P = .021$]). Knees with ACL laxity: 6-month (3 injection) data revealed no significant improvement. However, Hotelling multivariate analysis of paired values at 0 and 12 months for pain, swelling, joint flexion, and joint laxity in the dextrose-treated knees, revealed a statistically significant improvement ($P = .021$). Individual paired t tests indicated that blinded measurement of goniometric knee flexion range improved by 12.8 degrees ($P = .005$), and ADD improved by 57% ($P = .025$). Eight out of 13 dextrose-treated knees with ACL laxity were no longer lax at the conclusion of 1 year. CONCLUSION: Prolotherapy injection with 10% dextrose resulted in clinically and statistically significant improvements in knee osteoarthritis. Preliminary blinded radiographic readings (1-year films,

with 3-year total follow-up period planned) demonstrated improvement in several measures of osteoarthritis severity. ACL laxity, when present in these osteoarthritic patients, improved.

Reeves KD, Hassanein K (2000). 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* 6(4): 311-20.

OBJECTIVES: To determine the clinical benefit of dextrose prolotherapy (injection of growth factors or growth factor stimulators) in osteoarthritic finger joints. DESIGN: Prospective randomized double-blind placebo-controlled trial. SETTINGS/LOCATION: Outpatient physical medicine clinic. SUBJECTS: Six months of pain history was required in each joint studied as well as one of the following: grade 2 or 3 osteophyte, grade 2 or 3 joint narrowing, or grade 1 osteophyte plus grade 1 joint narrowing. Distal interphalangeal (DIP), proximal interphalangeal (PIP), and trapeziometacarpal (thumb CMC) joints were eligible. Thirteen patients (with seventy-four symptomatic osteoarthritic joints) received active treatment, and fourteen patients (with seventy-six symptomatic osteoarthritic joints) served as controls. INTERVENTION: One half milliliter (0.5 mL) of either 10% dextrose and 0.075% xylocaine in bacteriostatic water (active solution) or 0.075% xylocaine in bacteriostatic water (control solution) was injected on medial and lateral aspects of each affected joint. This was done at 0, 2, and 4 months with assessment at 6 months after first injection. OUTCOME MEASURES: One-hundred millimeter (100 mm) Visual Analogue Scale (VAS) for pain at rest, pain with joint movement and pain with grip, and goniometrically-measured joint flexion. RESULTS: Pain at rest and with grip improved more in the dextrose group but not significantly. Improvement in pain with movement of fingers improved significantly more in the dextrose group (42% versus 15% with a p value of .027). Flexion range of motion improved more in the dextrose group (p = .003). Side effects were minimal. CONCLUSION: Dextrose prolotherapy was clinically effective and safe in the treatment of pain with joint movement and range limitation in osteoarthritic finger joints.

Reeves KD, Hassanein KM (2003). Long-term effects of dextrose prolotherapy for anterior cruciate ligament laxity. *Altern Ther Health Med* 9(3): 58-62.

CONTEXT: Use of dextrose prolotherapy. Prolotherapy is defined as injection that causes growth of normal cells or tissue. OBJECTIVE: Determine the 1 and 3 year efficacy of dextrose injection prolotherapy on anterior cruciate ligament (ACL) laxity. After year 1, determine patient tolerance of a stronger dextrose concentration (25% versus 10%). DESIGN: Prospective consecutive patient trial. SETTING: Outpatient physical medicine clinic. PATIENTS OR OTHER PARTICIPANTS: Eighteen patients with 6 months or more of knee pain plus ACL knee laxity. This laxity was defined by a KT1000 anterior displacement difference (ADD) of 2 mm or more. INTERVENTION: Intraarticular injection of 6-9 cc of 10% dextrose at months 0, 2, 4, 6, and 10. Injection with 6 cc of 25% dextrose at 12 months. Then, depending on patient preference, injection of either 10% or 25% dextrose every 2-4 months (based on patient preference) through 36 months. MAIN OUTCOME MEASURES: Visual analogue scale (VAS) for pain at rest, pain on level surfaces, pain on stairs, and swelling. Goniometric flexion range of motion, and KT1000-measured ADD were also measured. All measurements were obtained at 0, 6, 12 and 36 months. RESULTS: Two patients did not reach 6 month data collection, 1 of whom was diagnosed with disseminated cancer. The second was wheelchair-bound and found long-distance travel to the clinic problematic. Sixteen subjects were available for data analysis. KT1000 ADD, measurement indicated that 6 knees measured as normal (not loose) after 6 months, 9 measured as normal after 1 year (6 injections), and 10 measured as normal at 3 years. At the 3 year follow-up, pain at rest, pain with walking, and pain with stair use had improved by 45%, 43%, and 35% respectively. Individual paired t tests indicated subjective swelling improved

63% ($P = .017$), flexion range of motion improved by 10.5 degrees ($P = .002$), and KT1000 ADD improved by 71% ($P = .002$). Eleven out of 16 patients preferred 10% dextrose injection. **CONCLUSION:** In patients with symptomatic anterior cruciate ligament laxity, intermittent dextrose injection resulted in clinically and statistically significant improvement in ACL laxity, pain, swelling, and knee range of motion.

Scarpone M, Rabago DP, et al. (2008). The efficacy of prolotherapy for lateral epicondylitis: a pilot study. Clin J Sport Med **18**(3): 248-54.

OBJECTIVES: To assess whether prolotherapy, an injection-based therapy, improves elbow pain, grip strength, and extension strength in patients with lateral epicondylitis. **SETTING:** Outpatient Sport Medicine clinic. **STUDY DESIGN:** Double-blind randomized controlled trial. **PARTICIPANTS:** Twenty-four adults with at least 6 months of refractory lateral epicondylitis. **INTERVENTION:** Prolotherapy participants received injections of a solution made from 1 part 5% sodium morrhuate, 1.5 parts 50% dextrose, 0.5 parts 4% lidocaine, 0.5 parts 0.5% sensorcaine and 3.5 parts normal saline. Controls received injections of 0.9% saline. Three 0.5-mL injections were made at the supracondylar ridge, lateral epicondyle, and annular ligament at baseline and at 4 and 8 weeks. **OUTCOME MEASURES:** The primary outcome was resting elbow pain (0 to 10 Likert scale). Secondary outcomes were extension and grip strength. Each was performed at baseline and at 8 and 16 weeks. One-year follow-up included pain assessment and effect of pain on activities of daily living. **RESULTS:** The groups were similar at baseline. Compared to Controls, Prolotherapy subjects reported improved pain scores (4.5 +/- 1.7, 3.6 +/- 1.2, and 3.5 +/- 1.5 versus 5.1 +/- 0.8, 3.3 +/- 0.9, and 0.5 +/- 0.4 at baseline and at 8 and 16 weeks, respectively). At 16 weeks, these differences were significant compared to baseline scores within and among groups ($P < 0.001$). Prolotherapy subjects also reported improved extension strength compared to Controls ($P < 0.01$) and improved grip strength compared to baseline ($P < 0.05$). Clinical improvement in Prolotherapy group subjects was maintained at 52 weeks. There were no adverse events. **CONCLUSIONS:** Prolotherapy with dextrose and sodium morrhuate was well tolerated, effectively decreased elbow pain, and improved strength testing in subjects with refractory lateral epicondylitis compared to Control group injections.

Staal JB, de Bie R, et al. (2008). Injection therapy for subacute and chronic low-back pain. Cochrane Database Syst Rev(3): CD001824.

BACKGROUND: The effectiveness of injection therapy for low-back pain is still debatable. Heterogeneity of target tissue, pharmacological agent and dosage generally found in randomized controlled trials (RCTs) points to the need for clinically valid comparisons in a literature synthesis. **OBJECTIVES:** To determine if injection therapy is more effective than placebo or other treatments for patients with subacute or chronic low-back pain. **SEARCH STRATEGY:** We updated the search of the earlier systematic review and searched the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE databases from January 1999 to March 2007 for relevant trials reported in English, French, German, Dutch and Nordic languages. We also screened references from trials identified. **SELECTION CRITERIA:** RCTs on the effects of injection therapy involving epidural, facet or local sites for subacute or chronic low-back pain were included. Studies which compared the effects of intradiscal injections, prolotherapy or Ozone therapy with other treatments, were excluded unless injection therapy with another pharmaceutical agent (no placebo treatment) was part of one of the treatment arms. Studies about injections in sacroiliac joints and studies evaluating the effects of epidural steroids for radicular pain were also excluded. **DATA COLLECTION AND ANALYSIS:** Two review authors independently assessed the quality of the trials. If study data were clinically and statistically too heterogeneous to perform a meta-analysis, we used a best evidence synthesis to summarize the results. The evidence was

classified into five levels (strong, moderate, limited, conflicting or no evidence), taking into account the methodological quality of the studies. MAIN RESULTS: 18 trials (1179 participants) were included in this updated review. The injection sites varied from epidural sites and facet joints (i.e. intra-articular injections, peri-articular injections and nerve blocks) to local sites (i.e. tender- and trigger points). The drugs that were studied consisted of corticosteroids, local anesthetics and a variety of other drugs. The methodological quality of the trials was limited with 10 out of 18 trials rated as having a high methodological quality. Statistical pooling was not possible due to clinical heterogeneity in the trials. Overall, the results indicated that there is no strong evidence for or against the use of any type of injection therapy. AUTHORS' CONCLUSIONS: There is insufficient evidence to support the use of injection therapy in subacute and chronic low-back pain. However, it cannot be ruled out that specific subgroups of patients may respond to a specific type of injection therapy.

Topol GA, Reeves KD, et al. (2005). Efficacy of dextrose prolotherapy in elite male kicking-sport athletes with chronic groin pain. Arch Phys Med Rehabil **86**(4): 697-702.

OBJECTIVE: To determine the efficacy of simple dextrose prolotherapy in elite kicking-sport athletes with chronic groin pain from osteitis pubis and/or adductor tendinopathy. DESIGN: Consecutive case series. SETTING: Orthopedic and trauma institute in Argentina. PARTICIPANTS: Twenty-two rugby and 2 soccer players with chronic groin pain that prevented full sports participation and who were nonresponsive both to therapy and to a graded reintroduction into sports activity. INTERVENTION: Monthly injection of 12.5% dextrose and 0.5% lidocaine into the thigh adductor origins, suprapubic abdominal insertions, and symphysis pubis, depending on palpation tenderness. Injections were given until complete resolution of pain or lack of improvement for 2 consecutive treatments. MAIN OUTCOME MEASURES: Visual analog scale (VAS) for pain with sports and the Nirschl Pain Phase Scale (NPPS), a measure of functional impairment from pain. RESULTS: The final data collection point was 6 to 32 months after treatment (mean, 17 mo). A mean of 2.8 treatments were given. The mean reduction in pain during sports, as measured by the VAS, improved from 6.3+/-1.4 to 1.0+/-2.4 (P <.001), and the mean reduction in NPPS score improved from 5.3+/-0.7 to 0.8+/-1.9 (P <.001). Twenty of 24 patients had no pain and 22 of 24 were unrestricted with sports at final data collection. CONCLUSIONS: Dextrose prolotherapy showed marked efficacy for chronic groin pain in this group of elite rugby and soccer athletes.

Yelland MJ, Mar C, et al. (2004). Prolotherapy injections for chronic low-back pain. Cochrane Database Syst Rev(2): CD004059.

BACKGROUND: Prolotherapy is an injection-based treatment for chronic low-back pain. Proponents of prolotherapy suggest that some back pain stems from weakened or damaged ligaments. Repeatedly injecting them with irritant solutions is believed to strengthen the ligaments and reduce pain and disability. Prolotherapy protocols usually include co-interventions to enhance the effectiveness of the injections. OBJECTIVES: To determine the efficacy of prolotherapy injections in adults with chronic low-back pain. SEARCH STRATEGY: We searched CENTRAL (2004, issue 1), MEDLINE, EMBASE, CINAHL and Science Citation Index from their respective beginnings to January 2004, with no restrictions on language. We consulted content experts to ensure we had not missed any references. SELECTION CRITERIA: Randomised and quasi-randomised controlled trials comparing prolotherapy injections to control injections, either alone or in combination with other treatments, were included. Studies had to include measures of pain and disability before and after the intervention. DATA COLLECTION AND ANALYSIS: Two reviewers independently selected the trials and assessed them for methodological quality. Treatment and control group protocols varied from study to study, making meta-analysis impossible.

MAIN RESULTS: We included four high quality studies with a total of 344 participants. All trials measured pain and disability levels at six months, three measured the proportion of participants reporting a greater than 50% reduction in pain or disability scores from baseline to six months. Two studies showed significant differences between the treatment and control groups for those reporting over 50% reduction in pain or disability. Their results could not be pooled. In one, co-interventions confounded interpretation of results; in the other, there was no significant difference in mean pain and disability scores between the groups. In the third study, there was little or no difference between groups in the number of individuals who reported over 50% improvement in pain and disability. The fourth study reporting only mean pain and disability scores showed no differences between groups. **REVIEWERS'**

CONCLUSIONS: There is conflicting evidence regarding the efficacy of prolotherapy injections in reducing pain and disability in patients with chronic low-back pain. Conclusions are confounded by clinical heterogeneity amongst studies and by the presence of co-interventions. There was no evidence that prolotherapy injections alone were more effective than control injections alone. However, in the presence of co-interventions, prolotherapy injections were more effective than control injections, more so when both injections and co-interventions were controlled concurrently.
