

# Dextrose Prolotherapy

## A Narrative Review of Basic Science, Clinical Research, and Best Treatment Recommendations



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### KEYWORDS

- Prolotherapy • Dextrose • Regenerative medicine • Osteoarthritis, Knee
- Tendinopathy

### KEY POINTS

- Animal models suggest specific tissue responses to hypertonic dextrose, including proliferation.
- Clinical benefit in human studies is not explained by proliferation alone; the mechanism of dextrose prolotherapy (DPT) is likely multifactorial.
- DPT is efficacious for knee osteoarthritis and likely efficacious for finger osteoarthritis and Osgood-Schlatter disease.
- Moderate-quality randomized clinical trial (RCT) evidence supports use of DPT in rotator cuff tendinopathy, lateral epicondylitis, plantar fasciopathy and nonsurgical sacroiliac pain.

### INTRODUCTION

Prolotherapy is an injection-based treatment of chronic musculoskeletal pain. A general surgeon in the United States, George Hackett, formalized injection protocols in the 1950s, based on 30 years of clinical experience.<sup>1</sup> Prolotherapy has been identified as a regenerative injection therapy<sup>2</sup> but is differentiated from other regenerative injection therapies, such as platelet-rich plasma (PRP) and stem cell injection by the absence of a biologic agent.

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Prolotherapy is increasingly popular in the United States and internationally. The current number of practitioners of prolotherapy in the United States is estimated as several thousand based on conference attendance and physician listings on relevant Web sites, including both independent physicians and members of multispecialty groups. Currently, Prolotherapy Regenerative Medicine is one of the 23 specialty colleges of the American Osteopathic Association (<http://www.prolotherapycollege.org>). Training of doctors of medicine and doctors of osteopathy is primarily outside medical schools, for example, through postgraduate-level conferences and service learning projects through universities, professional organizations, and foundations ([www.fammed.wisc.edu/prolotherapy](http://www.fammed.wisc.edu/prolotherapy), [www.aomed.org](http://www.aomed.org), and [www.hacketthemwallpatterson.org](http://www.hacketthemwallpatterson.org)).

Hypertonic dextrose is the most commonly used prolotherapy solution, with favorable outcomes shown in multiple clinical trials.<sup>3</sup> It is inexpensive, readily available, and reported to be safe. This review focuses on the basic science and clinical evidence of prolotherapy using hypertonic dextrose solutions. The term *dextrose* is interchangeable with *glucose* because dextrose is the dexter (right-handed) form of glucose found in animals and humans. For this discussion, the term dextrose is preferred.

## METHODS

A search of electronic databases was performed by the University of Kansas library staff, including Medline, Web of Science, and [ClinicalTrials.gov](http://ClinicalTrials.gov), from 1980 to 2016, without language restrictions. Search specifics included (1) prolotherapy; (2) (regenerative OR tendon OR tendinopathy OR ligament OR osteoarthritis) AND (dextrose OR glucose); and (3) dextrose injection from 1980 to 2016. Basic science studies were included in this review if they featured blinded histologic, histochemical, or radiographic outcome assessment. Clinical studies were included if randomized assignment was used and a dextrose arm was included. The strength of each RCT was assessed by 2 reviewers (K.D.R. and R.W.S.S.) using the Cochrane risk of bias tool.<sup>4</sup> Disagreements were resolved by consensus and presented in descriptive and tabled form.

## RESULTS

Of 469 studies identified, 48 met inclusion criteria and were grouped into the following 2 areas: basic science (n = 33) and clinical research (n = 15).

### **Basic Science Findings**

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#### ***In vitro effects of dextrose on cytokine levels***

Transport of dextrose into human cells uses a family of transport proteins, GLUTs 1–4, that interact with cytokines in a crucial way to signal either cell growth or repair.<sup>5</sup> DNA expression changes favoring production of multiple cytokines have been measured within 20 minutes of exposure to in vitro elevation of pericellular dextrose levels to as little as 30 mM (0.54%)<sup>6</sup> in a variety of animal and human cells, including fibroblasts,<sup>6–10</sup> chondrocytes,<sup>11,12</sup> and nerve cells.<sup>13,14</sup>

Proliferative tissue changes in diabetic patients who have frequent elevations of pericellular dextrose in the 30-mM range are prominent, such as with diabetic proliferative retinopathy.<sup>15</sup> Such effects are of unclear significance, however, given that elevated glucose levels in cases of diabetes seem to trigger interrelated complex pathophysiological mechanisms,<sup>15</sup> which may vary greatly from the effect of brief and isolated dextrose elevation on injection in either nondiabetics or diabetics. For example, the duration of glucose elevation is important to production of favorable<sup>16</sup> or unfavorable cytokines.<sup>17</sup>

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