

Evidence-Based Regenerative Injection Therapy (Prolotherapy) in Sports Medicine

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KEY POINTS

- The treatment of sports injuries to the point of restoration of full sports performance is an obvious goal in sports medicine. However, healing is the preferred goal because returning connective tissue to normal strength allows for a durable return to full sports performance.
- Regenerative injection therapy (prolotherapy) is the injection of growth factors or growth factor production stimulants to promote the regeneration of normal cells and tissue. Inflammation is not required, and scarring is not the result.
- Open-label clinical trials have been uniformly positive in outcome, but double-blind clinical trials have been hampered by a needling control that does not appear to be a placebo. Recent studies are making use of a noninjection control.
- Making use of consecutive patient data from athletes with career-threatening injuries (i.e., chronic groin strain in soccer or rugby players) that are not responsive to other treatments is a recommended study approach to assess regenerative injection therapy's ability to reverse otherwise permanent conditions. This is an avenue for the critical assessment of regenerative injection therapy's potential.
- Serial high-resolution ultrasound images are limited somewhat by uniformity of technique, but they offer a way to follow healing from regenerative injections.

INTRODUCTION

The treatment of sports injuries to the point of restoration of full sports performance is an obvious goal in sports medicine. Healing, however, is the preferred goal because returning connective tissue to normal strength allows for a durable return to full sports performance.

Given the advancements in the knowledge of the degenerative nature of chronic sprain or strain and the ability of high-definition ultrasound to demonstrate the objective healing of soft tissue, the

use of prolotherapy, which is also called *regenerative injection therapy* (RIT), is expected to greatly accelerate in the next decade. This chapter will cover the pathology of injury; the current treatment methods and their limitations; and the rationale, basic science, and clinical studies of prolotherapy/RIT. In the latter section, it will also introduce two areas of particularly pertinent research approaches in sports medicine: the treatment of connective-tissue-based, career-threatening injuries and the use of high-resolution ultrasound to document healing.

PATHOLOGY OF INJURY

During sports participations, tendons are subjected to unpredictable mechanical loads as they transmit forces to bone. Ligaments are likewise unpredictably stressed as they attempt to hold bony structures together at a fixed length. These mechanical loads, when excessive, lead to unhealthy changes in tendon or ligament structures. Numerous terms have been used to describe these unhealthy changes. *Tendinitis* implies inflammation, and *tendinosis* implies degeneration. Because inflammation and degeneration can only be confirmed via biopsy, the generic term *tendinopathy* is proposed as perhaps the best descriptive term.¹

Mechanical testing of tendon specimens has provided a stress-strain curve, and this curve demonstrates that collagen fibers uncrimp by 2% stretch of a tendon and microscopically rupture beginning at 4% to 8% stretch. Beyond 8% stretch, macroscopic tears are noted, and, beyond 12%, complete rupture is likely.¹ Repetitive submaximal loading can cause microscopic injuries that, through the failure of individual collagen fibers, reduce the effective cross-sectional area of the tendon or ligament and thus make it more susceptible to failure.²

CURRENT TREATMENT METHODS AND THEIR LIMITATIONS

Although the structure, composition, and mechanical properties of the tendon can change favorably in response to altered mechanical