# Platelet-Rich Plasma

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CME Continuing Medical Education

Several injectable substances have been studied for the treatment of tendinitis of the hand, wrist, and elbow, including corticosteroids, botulinum toxin, autologous blood, and platelet-rich plasma (PRP).[1–8] Whereas empiric data suggest a beneficial effect of many treatments for tendinitis, defined roles for these various injections remain unclear. For several years, orthopedic surgeons have used PRP to treat conditions such as tendinitis about the knee, hip, and shoulder[9–11]; however, data are inconclusive as to its precise mechanism of action as well as whether it demonstrates lasting benefit. We review the composition and preparation of PRP and list several of the available kits for its preparation.

## BACKGROUND

Blood consists of cellular elements (erythrocytes, leukocytes, and platelets) and plasma (the liquid component of blood that is predominantly water but also contains clotting factors, proteins, glucose, minerals, carbon dioxide, and oxygen). Platelets are nonnucleated blood cells that originate as megakaryocyte fragments and circulate throughout the body to provide hemostasis by means of clot formation. So-called "platelet-rich plasma" represents the patient's own plasma that has been mechanically treated to increase the concentration of platelets compared to whole blood. The supraphysiological concentration of platelets will provide a locally increased concentration of growth factors and cytokines that are contained within the platelets themselves.[9–11]

A local injection of PRP is, therefore, believed to work by releasing growth factors and cytokines that recruit reparative cells and enhance the healing process at the injection site.[2,3,8–10] There is *in vitro* evidence to support growth factor stimulation of tendon healing.[12] However, the exact growth factors and cytokines that are liberated, the precise mechanisms of action, the time courses of release and clearance, and the effects on both normal and abnormal tissues *in vivo* remain unclear.

During the past decade, PRP has been used with increasing frequency in the musculoskeletal system for the augmentation of bone grafts, treatment of knee osteoarthritis, supplementation of rotator cuff repairs, reconstructions of the anterior cruciate ligament, and management of patellar tendinopathy, plantar fasciitis, Achilles tendinosis, and refractory elbow epicondylitis.[2,3,8,9] Many of the studies that have sought to support PRP injection are observational in nature and, therefore, have not provided conclusive evidence in favor of its routine use. However, well-designed outcome studies are emerging that show a potentially promising role for PRP in the management of chronic lateral epicondylitis.[3,5,8]

## PREPARATION AND CLASSIFICATION

At least 16 commercial PRP preparation systems are currently available (Table 1).[13] A sample of peripheral venous blood is drawn and immediately spun in a centrifuge to separate the erythrocytes from the platelets and leukocytes. The increased density of the erythrocytes causes them to sink to the bottom of the centrifuge tube more rapidly than do the platelets and leukocytes. Further concentration then isolates PRP from platelet-poor plasma (Fig. 1).[9] Commercially available PRP kits concentrate platelets in the final injectate up to 9 times the normal concentration found in whole blood. The resultant volume of PRP and the final platelet and leukocyte concentrations differ among preparation systems.[9]

Dohan Ehrenfest et al[14] categorized PRP based on leukocyte and fibrin content. Mishra et al[11] classified PRP according to the platelet concentration, the presence of leukocytes, and the inclusion of an activator (Table 2).[15] Platelets will increase anabolic signal-

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ing, whereas leukocytes might release higher concentrations of catabolic signaling molecules.[16] Exogenous platelet activators include calcium chloride and thrombin; both substances induce fibrin and create a putty-like or gel-like clot.[9] The addition of an activator to PRP can diminish efficacy by decreasing the long-term availability of growth factors.[17] Delivery of PRP without an activator is feasible because platelets are triggered to release growth factors and cytokines by exposure to tendon-derived collagen.[2,3,9,17]

## SAFETY

Given the autologous nature of PRP, safety concerns are minimal at this time. There have been reports of localized reactions to exogenous proteins such as fibrin. Nevertheless, the reported complications in most clinical series have been limited to transient pain and inflammation at the injection site.[9,10,18] One laboratory study found that PRP has an antimicrobial effect against *Staphylococcus aureus* and *Escherichia coli*, potentially diminishing the risk for infection with these organisms.[19] Platelet-rich plasma is still considered investigational by many insurance carriers; consequently, there is an uncertain effect on the cost of treatment.

Platelet-rich plasma represents a supraphysiological concentration of platelets that is thought to work by delivering a locally increased concentration of growth factors and cytokines to damaged tissue, potentially stimulating soft tissue healing. Understanding the differences in PRP preparations is essential when interpreting clinical studies and considering concentrated platelets as a therapeutic option. Large prospective and randomized studies are necessary to investigate the efficacy of different preparations of PRP, controlling for hematologic differences between patients (eg, platelet and leukocyte counts) and postinjection rehabilitation protocols.

### EDUCATIONAL OBJECTIVES

- State the components of plasma.
- Discuss the platelet-rich plasma mechanisms of action with regard to healing tissue.
- Describe the preparation of platelet-rich plasma.
- Discuss the differences among platelet-rich plasma preparations.
- State the various exogenous and endogenous platelet activators.
- List complications associated with the use of platelet-rich plasma injections.

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**TABLE 1. Representative Platelet-Rich Plasma Therapy Preparation Systems***

| System | Volume of Blood (mL) | Final PRP Volume (mL) | Final Platelet Concentration (Compared With Whole Blood) | Available Activator | Leukocyte Concentration ($\times 10^3/\mu L$) (Compared With Whole Blood) | Fibrinogen (mg/dL) |
|---|---|---|---|---|---|---|
| Autologous conditioned plasma (Arthrex, Naples, FL) | 9 | 3–5 | 2–3× | None | N/A | N/A |
| Cascade (Musculoskeletal Tissue Foundation, Edison, NJ) | 9 or 18 | 2 or 4 | 1.6×† | Calcium | 1.1 ± 0.2† (6-fold) | 283.8 ± 34.2† |
| GPS III (Biomet, Warsaw, IN) | 27 or 54 | 3 or 6 | 2.1–9.3×‡ | Calcium chloride/ thrombin | 34.4 ± 13.6† (5-fold) | 286.0 ± 42.7† |
| SmartPReP (Harvest Technologies, Plymouth, MA) | 20 or 60 | 3 or 7 | 4.4–7.6× | Thrombin | N/A | N/A |
| Magellan (Arteriocyte Inc, Cleveland, OH)† | 30, 45, or 60† | Variable§ | 2.8–14×§ | N/A§ | 11.0 ± 8.2§ (2-fold) | 277.4 ± 30.5§ |

N/A, not available.
*Data obtained from Hall et al,[9] except as otherwise noted.
†Data obtained from Castillo et al.[13]
‡Data obtained from manufacturer (http://www.biomet.com/biologics/information/pdf/BBI0003.0.pdf) and Castillo et al.[13]
§Data obtained from manufacturer (http://arteriocyte.com/amsi/professionals/Product_Magellan_Overview.asp) and Castillo et al.[13]

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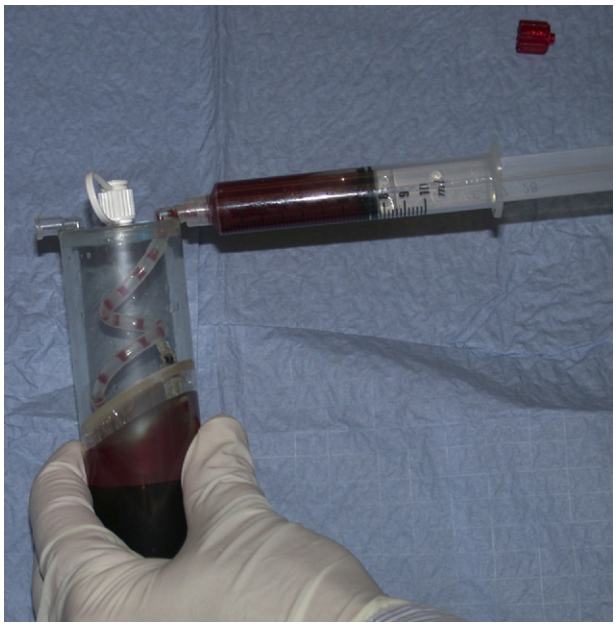

**FIGURE 1:** Extraction of platelet-rich plasma after withdrawing and discarding the platelet-poor plasma layer (GPS III, Biomet, Warsaw, IN).

**TABLE 2. Mishra's Platelet-Rich Plasma Classification System[11,15]**

| Type | Leukocyte Concentration | Activated |
|---|---|---|
| 1 (A or B) | Increased over patient's baseline | No |
| 2 (A or B) | Increased over patient's baseline | Yes |
| 3 (A or B) | Few or no leukocytes | No |
| 4 (A or B) | Few or no leukocytes | Yes |

A, platelet concentration ≥ 5× patient's baseline; B, platelet concentration ≤ 5× patient's baseline.


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