

# Platelet-Rich Plasma— Does It Really Work?

While the jury is still out, this biological treatment shows great promise.

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In response to an injury or tissue damage, the body recruits platelets and white blood cells from the blood to initiate a well-organized and complex series of events where proteins act as messengers to regulate the healing process. Many proteins are derived from small cell fragments in the blood called platelets.

Platelets are formed in the bone marrow and, in a resting state, freely move in the bloodstream. When an injury occurs, these platelets become activated and begin to aggregate at the site of the injury to release stored beneficial proteins referred to as growth factors.

Outside the bloodstream platelets become activated and release prolif-

erative and morphogenic proteins. These growth factors work synergistically to invoke the following benefits: induce proliferation and differentiation of various cell types, e.g., stem cells, osteoblasts, and epidermal cells. These growth factors enhance and modulate production of collagen and Tissue Inhibitor of metalloproteinases (TIMP). They also stimulate angiogenesis and chemotaxis.

Blood contains plasma, red blood cells, white blood cells and platelets.

1987 in open heart surgery.<sup>2</sup> Today, platelet-rich plasma injections have been used safely in many fields including: sports medicine, orthopedics, cosmetics, and urology.

There are a number of growth factors which contribute to the healing process. The first is PDGF-aa, PDGF-ab, and PDGF-bb. This growth factor stimulates cell replication, promotes angiogenesis, promotes epithelialization, and promotes granulation tissue formation. The second is trans-

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Within, the platelets contain granules which contain clotting and growth factors. During the healing process, the platelets are activated and aggregate together. They then release the granules, which stimulate the inflammatory cascade and healing process.<sup>1</sup>

## **ACP and PRP**

Autologous conditioned plasma (ACP) is a concentration of platelets and growth factors created from a patient's own blood. Increased levels of growth factors improve signaling and recruitment of cells to the site of injury, and enhance the environment for healing.

Autologous platelet-rich plasma (PRP) injections were first used in

forming growth factor (TGF-b1, TGF-b2). This growth factor promotes formation of extracellular matrix, and regulates bone cell metabolism. The third, vascular endothelial growth factor (VEGF), promotes angiogenesis. The fourth, epidermal growth factor (EGF), promotes cell differentiation, and stimulates re-epithelialization. The fifth is fibroblast growth factor (FGF), which promotes proliferation of endothelial cells and fibroblasts, as well as stimulation of angiogenesis.

Blood typically contains six percent platelets, whereas PRP has a significantly increased supra-physiological platelet concentration. These platelet concentration levels can vary depend-

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ing on the method of extraction. Studies have shown that the clinical benefit can be obtained if the PRP used has an increased platelet concentration of 4X greater than normal blood.<sup>3</sup> This can increase the concentration of platelets and growth factors up to 600%.

The future of medicine and orthopedics is increasingly looking to gene therapy and utilizing “biologic” solutions to common problems such as bone, ligament, cartilage, and tendon healing.

The Food and Drug Administration has approved the use of PRP in other applications within the field of orthopedic surgery. Research and clinical data show that PRP injections are extremely safe, and that there is minimal risk for any adverse reaction or complication. There is always a small risk of infection from any injection but it usually is very rare. Recent research suggests that PRP may have an anti-bacterial property which protects against possible infection.<sup>4</sup> At the present time, FDA approval of PRP is pending, and these injections are considered “off-label use.” On the other hand, PRP is not an artificial or manufactured product that requires long-term safety evaluation. Initially, the use of platelet-rich plasma was banned by the World Anti-Doping Agency (WADA) because it is a blood substance. WADA has recently allowed the injection of PRP directly into a muscle.

## Conditions and Candidates

What are some of the conditions that can be treated with platelet-rich plasma? It can be used for knee pain, patellar tendinitis/tendinosis, quadriceps muscle injuries, ligament sprains or tears, and bursitis. It also has use in hip pain, hip girdle muscle pain or injury, piriformis injury, greater trochanteric bursitis, ischial bursitis, pubic symphysis pain, sacroiliac joint pain, and hamstring tendonitis or tears. It is used for shoulder and arm pain: rotator cuff tendonitis, tendonopathy, or partial tears, acromio-clavicular joint pain or arthritis, bicipital tendonitis, medial and lateral epicondylitis



Figure 1: Collecting blood after centrifuging down the platelet-rich plasma.

(golfer's and tennis elbow); for back pain: spinal nerve inflammation, facet joint arthritis, disc herniation or tear, and interspinous ligament sprain; for lower leg and foot pain: plantar fasci-

gies. These candidates should have significant symptoms, so that surgical intervention has been considered.

Those patients who are not considered good candidates for PRP injections include: patients who are on anticoagulant therapy for medical conditions such as history of DVT, or atrial fibrillation and are unable to cease their medication for PRP injections. Others include patients who are unable to remain off of aspirin or other anti-inflammatory medications before or after the procedure, patients who will not allow removal and injection of blood products into their bodies, and patients who are allergic to lidocaine or other local anesthetics.

Following a physical examination and diagnostic workup, the podiatric physician will determine if the PRP will benefit the patient based on the injury. In preparation of the PRP injection, patients should stop all an-

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itis, shin splints, peroneal tendonitis, ankle sprains, and Achilles tendonitis or partial tears.

A candidate for platelet-rich plasma injections is an adult patient who has had chronic pain with tendonitis, tenosynovitis, or other conditions, and 1) who failed previous treatment, and 2) or has the inability to tolerate oral anti-inflammatory medications due to medical conditions or aller-

ti-inflammatory medications for one week prior to the procedure. This includes aspirin (regular and mini-dose 81 mg pills), ibuprofen, naproxen, and arthritis medication such as Celebrex, Arthrotec, Mobic, Voltaren, etc. Patients should be prepared to reduce activity for about 2 to 3 days after the injection.

## The Procedure

The procedure consists of drawing 30-50 cc. of blood from the patient's arm. It is prepared and placed in a sterile single use container where it is spun down in a high speed centrifuge. The platelet-rich plasma and white blood cells are then concentrated and collected in a sterile syringe (Figure 1). This increases the concentration of platelets and growth factors by up to 600%. Some of the blood is used to create an “activator” of the PRP. The area to be in-



Figure 2: Injection of platelet-rich plasma to the infra-calcaneal heel for chronic plantar fasciosis.

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jected is prepped using the standard sterile technique. The area is anesthetized proximally with either lidocaine or a combination of lidocaine and Marcaine. The tendon or fascia is then injected from 3-5 cc. of the platelet-rich plasma and activator.

Depending on the size of the injured tissue, one or several needles are inserted to optimize placement of the PRP (Figure 2, 3, 4). Depending on the severity and duration of the injury, one to three PRP injections are suggested. After the initial injection, the patient may feel an “achy” soreness at the site of the injury. This soreness is a positive sign that the healing response has begun. There is a protocol for post-injection that may involve the use of a walker boot and crutches for injections of the lower extremity. Ice should be applied to the area of the injection for about 20 minutes, 3 times/day for only the next 48 hours. The patient should be instructed not to take any anti-inflammatory medications for the next two weeks. They are contraindicated in these circumstances since these NSAIDs may block the intended healing response. For pain, acetaminophen or analgesic medication may be prescribed. Specific instructions regarding stretching and light resistance training is recommended, and a physical therapy program may be prescribed to enhance success of the treatment. No sports is recommended for at least the first three months, and then activities can be increased after that time until full return to activity.

Following the initial treatment, a follow-up visit takes place in two to three weeks, at which time an evaluation of the patient’s response is performed. At that time, a decision regarding the need for additional PRP injections may be made. Presently, there is no data to show that further injections may be beneficial.

## Clinical Studies

There have been a number of clinical studies involving platelet-rich plasma for Achilles tendinopathy, plantar fasciitis,



Figure 3: Injection of platelet-rich plasma to the posterior heel for chronic insertional Achilles tendinosis.

osteoarthritis of the knee, common peroneal nerve palsy, and its use in foot and ankle surgery. One study by Voss et al., entitled *Platelet-rich Plasma Injection for Chronic Achilles Tendinopathy: A Randomized Controlled Study* compared a control group (sa-

alogous platelet concentrate injections. Data was collected before the procedure, and again at 4, 8, 12, 26 weeks, and one year post-procedure. The main outcomes of the study involved pain and function, measured with questionnaires. Presently, the study has not been completed; however, their results should have great significance.<sup>6</sup>

Molloy, et al. in a study (the roles of growth factors in tendon and ligament healing) reported that the individual cytokines present in the platelet alpha-granules have been shown to enhance fibroblast migration and proliferation, up-regulate vascularization, and increase collagen deposition in a variety of in vitro and In vivo settings. They concluded that the cytokines present in platelet al-

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line injection) to the intervention group (PRP injection). Both groups utilized active treatment (eccentric exercises), with both groups having good results (74.6% vs. 70.9% respectively).<sup>5</sup> An ongoing study by Peerbooms, et al., *Use of platelet-rich plasma to treat plantar fasciitis: design of a multi-centre randomized controlled study*, 120 subjects with chronic plantar fasciitis randomly had either steroid injection or au-

pha-granules affect the healing stages necessary to reverse a chronic plantar fasciitis condition.<sup>7</sup>

In a preliminary, randomized study comparing cortisone injections and platelet-rich plasma injections for chronic plantar fasciosis, Achilles tendonosis, posterior tibial, and anterior tibial tenosynovitis, Ross reported the initial findings at the APMA National Meeting in 2012. In the study’s second year, 29 subjects (16 cortisone, 13 PRP injections) were studied. In the cortisone group 9 out of 16 had good results vs. 7 out of the 13 showed beneficial results from the PRP injections. There were a number of variables that can affect the outcome of the PRP injections. Some of those include: whether a night splint or orthotics were worn or not, if physical therapy, stretching and icing were performed or not, the injection technique, and if there was follow-up.



Figure 4: Injection of platelet-rich plasma to the medial ankle for chronic posterior tibial tenosynovitis.

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What were the advantages vs. disadvantages of cortisone vs. PRP injections? Platelet-rich plasma injections do not cause degeneration or inhibit the healing process, but rather activate the hormonal response. PRP is indicated for patients who have failed previous treatment, or are unable to tolerate p.o. NSAIDs. Cortisone injections reduce inflammation, can cause weakening of structures, and result in potential rupture. They typically mask the problem until the healing process begins. In conditions such as fasciosis and tendinosis, there is a decrease in the inflammatory response. There is a reduction in growth and healing factors, which causes more scar tissue formation, which inhibits the healing process. Cortisone injections have a better effect in the acute phase while there is an inflammatory process present.

Koerner, et al. reported on platelet-rich plasma and its uses in foot and ankle surgery. They reported the theoretical benefits of a biological adjunct like platelet-rich plasma in significantly enhancing fusion rates. In the study of high-risk diabetic patients who had been diagnosed 10 years prior to ankle, hind foot, and pantalar fusions, platelet-rich plasma was applied intra-operatively, and the patients were followed for either unions or non-unions. Four of the twelve patients went on to non-union after the procedure. Growth factors (PDGF-ab and VEGF) in the bone may affect the outcome of a successful arthrodesis in diabetic patients. The study supports the concept that growth factor levels within the fusion site of a diabetic patient may affect the outcome of a successful hind foot fusion.<sup>8</sup>

There have been a number of anecdotal studies and uses of platelet-rich plasma for sports medicine injuries. One of the best testimonials was by Dr. El Attrache. He said, "For the last several decades, we've been working on the mechanical effects of healing, the strongest constructs, can we put strong anchors in? But we've never been able to modulate the biology of healing. This is addressing the issue. It deserves a lot more study before we can say it works with proper

definitiveness. The word I would use is promising."

## Conclusions

We have been taught that if a patient has chronic inflammation from an overuse injury, then a cortisone injection was one of the treatments of choice. That thought process is becoming outdated. Using the body's own biological supply of growth factors and reparative cytokines has now become a new and ongoing philosophy in the treatment of overuse

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## Many studies are ongoing, while other studies reported good or mixed results.

and traumatic injury. Many studies are ongoing, while other studies reported good or mixed results. Therefore, the jury is still out, and it is still not clear if platelet-rich plasma is efficacious for plantar fasciosis and Achilles tendinosis. Continued research is necessary in order to make that determination. However, I do believe that we will see, in the near future, platelet-rich plasma injections or application in a more evolved, researched manner, the standard of choice for these injuries. This could be the next frontier in how medicine is applied to our patients. **PM**

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