# Platelet-Rich Plasma

**By Maureen Williams, ND**

Platelet-rich plasma (PRP) is a blood product obtained from centrifuged whole blood. Centrifuging causes a stratified settling of blood components in order of density, with red blood cells settling on the bottom, platelet-poor plasma at the top, and white blood cells and platelet-rich plasma in between. PRP was so named because its concentration of platelets is higher than in whole circulating blood.[1] In fact, the concentrations of platelets in PRP may be more than five times greater than those found in whole blood. In addition, PRP is estimated to contain more than 1,500 biologically active protein-based molecules.[2,3]

PRP was first used in the 1970s as a transfusion product for people with thrombocytopenia (a low number of platelets). PRP is now recognized as a source of plasma-derived fibrinogen and platelet-related growth factors, clotting factors, immune-modulating compounds, enzymes, and enzyme inhibitors that regulate local inflammatory responses as well as tissue growth and repair.[3,4] With strong evidence for its safety as an injection therapy,[2] PRP is being investigated for numerous possible benefits, including musculoskeletal and soft-tissue repair, cartilage regeneration, wound healing, hair growth promotion, and skin remodeling and rejuvenation.[1,5]

## PRP: Therapeutic Procedure and Safety

PRP is usually used as an autologous therapy; this means it is derived from the same person in whom it will be used, rather than a donor. PRP can be collected and administered in one office visit, since the entire procedure can be completed in approximately 30 minutes.

PRP is obtained by first drawing a small amount of blood from a vein. Anticoagulants such as citrate dextrose or sodium citrate are often added to prevent clotting in the blood tube. The whole-blood sample is processed using a centrifuge in order to separate PRP from the other blood components. Once isolated, PRP can be injected into target tissues such as arthritic joints, wounds, surgical sites, injured tissues, dysfunctional hair follicles, or aging skin. In some cases, activators are added before use. Injections are often done once, but sometimes PRP is applied in multiple injection sessions a week or more apart. The benefits of PRP therapy have been noted to persist for a year or longer.[6-8]

It is worthwhile to note that PRP is a novel therapeutic in need of standardization. Different methods for obtaining PRP are used and result in materials that vary in composition, each of which may have different clinical applications.[5] For example, some methods yield PRP that still contains white blood cells, while others yield a purer PRP; the presence of white blood cells may have advantages in some scenarios. PRP preparations can also be pre-activated by the addition of thrombin, or non-activated, in which case it is thought that contact with naturally present connective tissue components after injection trigger activation.[2,3,4] Standardization of centrifuge procedures, the use of anticoagulants during preparation, and platelet concentration targets could also help validate this field of research.[9]

PRP therapy has an excellent safety record[2]; however, infrequent adverse events have been reported as a result of PRP injections in both research and clinical practice. These include

localized infection, injury to nerves or blood vessels, localized swelling or pain, and scarring.[4] At least one case of allergic reaction, most likely to calcium citrate added to the injection solution, has been described.[10] In addition, a single report exists of a woman who developed irreversible blindness due to ischemia after PRP injection into her eyelid for cosmetic purposes.[11]

## Musculoskeletal and Soft Tissue Indications

As a source of large amounts of protein factors involved in tissue healing, PRP has attracted much interest for its potential uses in musculoskeletal and soft tissue injuries and disorders. PRP stimulates local migration, proliferation, and activation of fibroblasts—cells that produce collagen and other structural compounds needed for tissue repair. Factors in PRP also promote formation of new blood vessels and regulate inflammatory signaling, and have even been found to decrease pain, reduce use of pain medication, and improve sleep.[4]

**Osteoarthritis.** Intra-articular (into the joint) injections of PRP have been shown in multiple clinical trials to reduce pain and improve function in joints affected by early osteoarthritis. Its effects in arthritic joints may be mediated by inhibiting inflammation, promoting tissue regeneration, and reversing senescence (age-related cellular dysfunction) in the joint.[12]

Although PRP therapy has been found to reduce pain and improve joint function both short- and long-term, some studies have not found any benefits for PRP therapy in osteoarthritis. This may be due to lack of standardized protocols for PRP preparation and use. Nevertheless, PRP appears to be beneficial for treating osteoarthritis, particularly of the knee, and the likelihood of benefit is greater in those with milder degrees of degeneration.[13,14] In addition, a meta-analysis of trials comparing PRP to hyaluronic acid indicated PRP may be the more effective of these two approaches.[15]

**Tendon and ligament problems.** A number of studies have examined the effects of PRP therapy as a treatment for various tendon and ligament pathologies. Overall, the effect of PRP therapy on pain and function in people with these conditions appears to be marginal[16]; however, a growing body of evidence suggests it may lead to better long-term pain management relative to other therapies in certain conditions, specifically, rotator cuff (shoulder) and lateral epicondyle (elbow) pathologies.[17,18]

A recent meta-analysis of randomized controlled trials reviewed 21 reports that included a combined total of 1,031 participants with chronic tendinopathies. The analysis found that PRP reduces long-term tendinopathy pain, with strongest evidence in treating rotator cuff and lateral epicondyle pathologies.[19] In addition, some clinical trials suggest PRP reduces pain over the long term in those with patella (knee) tendinopathy.[20,21] Solid evidence for its usefulness in Achilles (ankle) tendinopathy is sparse.[22,23] In one clinical trial, 57 subjects with Achilles tendonitis were assigned to participate in a rehabilitation program combined with either four PRP injections two weeks apart, a single injection of methylprednisolone, or a single saline injection (placebo). This unusually high number of PRP treatments was found to be more effective than placebo, yet less effective than methylprednisolone, for relieving pain and improving function after 24 weeks of monitoring.[24]

**Plantar Fasciitis.** A number of studies have examined the possible role of PRP in treating plantar fasciitis. Although high-quality randomized controlled trials are limited, the evidence so far suggests PRP therapy may effectively reduce long-term plantar fasciitis pain better than steroid injections.[16] One meta-analysis of randomized controlled trials included ten studies with a combined total of 445 plantar fasciitis patients. The analysis showed PRP was more effective at reducing pain and improving foot and ankle function and alignment than other therapies (mainly steroid injections) one year after treatment.[25]

**Muscle injuries.** Traumatic injuries, genetic diseases, systemic conditions, and even aging can each contribute to muscle damage that might be responsive to PRP therapy.[26] Evidence shows PRP as a treatment for sports injuries may reduce inflammation and inhibit scarring, and some clinical trials suggest PRP combined with a rehabilitation program may shorten recovery time and improve pain relief without increasing re-injury risks; however, findings have been inconsistent and not statistically significant, indicating the need for further research.[26,27]

## Dermatologic Indications

Because of its ability to produce growth factors involved in skin repair and regeneration, PRP is believed by many to have a potential role in both medical and cosmetic skin care. Although numerous studies have investigated its ability to promote wound healing and reverse the effects of photoaging, this vein of research is plagued by the same issues as PRP research in general: namely, inconsistent methods for preparation and application of PRP.[9] Nevertheless, a growing number of reports suggest PRP may help to improve healing of chronic wounds, restore skin elasticity, reduce skin wrinkling and stretch marks, decrease scar tissue, and improve pigmentation of skin affected by vitiligo.[6,28,29]

**Skin Rejuvenation.** In a pilot trial, 20 middle-aged women with mildly photo-damaged skin received PRP injections into skin on the backs of their hands on three occasions 30 days apart. Six months after the beginning of treatment, wrinkling and elasticity had improved, and skin biopsies showed the treated tissue had a greater number of fibroblasts, more blood vessels, and higher collagen density.[30] In another trial, women with photoaged skin underwent a single session of PRP injections in one side of the face and normal saline in the other; six months later, participant ratings of skin texture and wrinkles were more improved for PRP-treated skin.[31] Three treatments with PRP injections led to improvements in skin color, firmness, and wrinkles in a pilot study with eleven participants.[32] Another preliminary trial documented increased firmness and elasticity of lower eyelid skin one month after three monthly treatments with PRP injections.[33] PRP has also been shown in preliminary trials to augment the effects of other skin rejuvenation therapies, such as microneedling (the insertion of fine, short needles into the skin to promote regenerative processes) and laser skin resurfacing.[34,35]

**Chronic ulcers.** A recent review included 12 studies with a combined total of 1,051 patients with chronic skin ulcers due to various causes. Despite inconsistencies in study methods, the review reported that both activated and non-activated topical PRP preparations, used once to twice per week for three to six weeks, have been shown to improve healing of ulcers and alleviate ulcer pain.[6] One preliminary trial included 104 participants with chronic, non-healing ulcers. Wound dressings with homologous PRP (from a matched donor) were applied twice

weekly up to ten times. Ulcers reduced in size after each dressing in all of the participants; in addition, ulcers were completely healed in 85 (81.73%) of the participants at the end of the final dressing.[36]

**Acute wound and burn healing.** Case reports and preclinical research suggest PRP may improve wound healing.[37-39] In a three-week controlled trial with 59 participants, acute traumatic wounds dressed with a PRP-based gel healed better than those dressed with Vaseline after the first week, and greater pain reduction was noted in those treated with PRP after two weeks.[40] A review of 13 articles exploring the use of PRP as part of acute wound treatment in a combined total of 982 participants concluded PRP can shorten wound healing and hospitalization times, decrease risk of complications, and may reduce pain.[41]

**Scars.** Several studies have examined the potential for PRP to be helpful in resolving scars from severe acne. Two recent reviews of these studies found the evidence to be most supportive for combined treatment with laser therapy and PRP, applied at two to three monthly sessions.[42,43]

**Vitiligo.** Vitiligo is a condition in which pigment-producing skin cells stop functioning or die, resulting in unpigmented skin patches. PRP injections may be helpful for promoting re-pigmentation in skin affected by vitiligo. In two controlled clinical trials, laser therapy plus PRP injections was more effective for improving re-pigmentation than either one alone or laser plus light (narrow-band UVB) therapy.[44,45] PRP has also been found to augment the effects of light therapy in patients with vitiligo.[46]

**Balding and hair loss.** Numerous randomized controlled trials have noted that PRP injections into the scalp in people with androgenetic alopecia (hormone-related hair loss) and alopecia areata (an autoimmune condition resulting in patches of hair loss) can increase hair numbers and density.[47-49] A recent review of research on PRP's effects on androgenetic alopecia included five randomized controlled trials. Despite differing methods and inconsistent findings, the authors of the review concluded PRP has a role, along with other therapies, in treating androgenetic hair loss.[50] In one trial, the combination of PRP injections plus topical 5% minoxidil and microneedling was more effective than minoxidil alone or minoxidil plus PRP at stimulating hair growth and increasing participant satisfaction.[51] Laser therapy has also been proposed as a possible adjunct to PRP treatment.[52] In patients with alopecia areata, PRP injections were found to be as effective as standard injection therapy using a corticosteroid.[53] According to one report, PRP may also improve outcomes of hair follicle transplantation.[54]

## Concluding Remarks

The tissue-restorative effects of PRP therapy have been demonstrated in numerous clinical trials. Preclinical research has provided insights into its mechanisms of action by showing that various molecules produced by PRP can increase local stem cell number and function, leading to tissue repair and regeneration.[55] Because of its apparent clinical usefulness, particularly in treating musculoskeletal and dermatologic conditions, as well as its high degree of safety, the development of standardized protocols for its preparation and application is warranted. One research group recommended a systematic approach to classification of PRP based on force, sequence, and time of centrifugation; baseline and final platelet concentrations; the use or non-

use of anticoagulants and activators during processing; and, the presence or absence of white blood cells in the final product.[9] Such an approach, along with consistent study designs, would allow for clear evidence confirming or refuting PRP's efficacy for specific indications.

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