### PLATELET-RICH PLASMA OVERVIEW

Platelet-rich plasma (PRP) is a blood-derived product that contains many elements shown to shorten recovery time and promote healing of a wide range of conditions ranging from osteoarthritis to lumbar radiculopathy to hair loss to erectile dysfunction (1, 2, 3, 4, 5, 6, 7, 8). Since the 1980s, PRP therapy has been used to accelerate wound healing in dentistry, bone healing in orthopedics and soft tissue healing following plastic surgery (9). More recently, however, PRP has been recognized as a regenerative therapeutic avenue with the potential to promote the initiation and progression of the body's innate healing responses. PRP contains high levels of platelets and growth factors that reduce inflammation and stimulate healing (2, 3). As an autologous blood-derived product, PRP has an extremely strong safety profile and involves little downtime postprocedure (10). Research has shown that PRP injections carry minimal risk of immune reaction or allergic reactions and that complications or side-effects from PRP procedures are extremely rare (9).

## **PRP COMPONENTS**

PRP contains many components thought to play major roles in wound healing, including platelets, growth factors and cytokines. Platelets are circulating cell fragments that are produced in the bone marrow. The function of platelets in the body is to form blood clots and prevent bleeding at injury sites. In response to injury, damaged blood vessels release signals that activate platelets. Platelets contain alpha-granules that are highly concentrated with many growth factors involved in tissue repair mechanisms. Upon activation, growth factors are released from platelet alpha-granules which then act on nearby cells to promote wound healing and repair (9). Several of these growth factors, such as platelet-derived growth factor, insulin-like growth factor, vascular endothelial growth factor and epidermal growth factor, are involved in initiating and promoting tissue repair mechanisms (3, 9).

In addition to releasing high concentrations of growth factors, activated platelets also release cytokines. Cytokines are signaling molecules that are involved in the modulation of inflammation and cell growth processes (11). The cytokines and growth factors released by activated platelets can act on many different cell types, including myocytes (muscle cells), tendon cells and bone cells, and can mediate tissue regeneration by stimulating cell proliferation and angiogenesis (formation of new blood vessels) (12). The high concentration of growth factors and cytokines found in PRP products can contribute to restoration of damaged connective tissue in myriad clinical applications.

### **PRP PREPARATION**

PRP therapy is a minimally invasive outpatient procedure performed under monitored care anesthesia (light sedation). To obtain PRP product, blood is drawn and is placed in a centrifuge machine. This processing results in the activation of the platelets in the blood sample and subsequent release of growth factors and cytokines from the platelet alpha-granules. Centrifugation activates the platelets and concentrates the growth factors and cytokines into a

product that can be injected directly into sites of injury. PRP therapy stimulates natural wound repair mechanisms to reduce pain and promote healing.

# **PRP APPLICATIONS**

The regenerative potential of PRP products has been shown to have profound therapeutic benefits in the treatment of many conditions. At Hudson Medical, we use PRP therapy to treat musculoskeletal injuries, androgenetic alopecia, and erectile dysfunction.

PRP therapy in the treatment of musculoskeletal injuries has been widely studied. As part of our regenerative medicine specialty, we offer PRP therapy to patients with osteoarthritis, spinal conditions (e.g. spinal radiculopathy, degenerative disc disease, spinal spondylosis), tendinopathy, and other joint and tendon-related conditions.

## **OSTEOARTHRITIS**

Extensive research supports the use of PRP therapy in osteoarthritis symptom relief. Osteoarthritis is a degenerative joint condition in which the cartilage at the end of bones deteriorates, causing pain, joint stiffness and inflammation. Osteoarthritis can affect any joints in the body but is most common in the knees, spine and hips (13). Traditional treatments for osteoarthritis primarily target symptom relief and include physical therapy, pharmacological analgesics (i.e. non-steroidal anti-inflammatory drugs, Paracetamol, opioids), steroid injections, and surgery. Recent interest in regenerative medicine prompted the discovery of PRP therapy as a treatment option for patients with osteoarthritis, as PRP therapy has been shown to significantly reduce joint pain (6, 7). Further, research has shown that PRP therapy results in more significant pain relief and improved function in patients with osteoarthritis when compared with traditional treatment options (14).

#### **SPINAL CONDITIONS**

Chronic back pain is one of the most common ailments in the United States (15). There are many different sources of chronic back pain ranging from spinal radiculopathy to spinal spondylosis to sacroiliac joint dysfunction. Spinal radiculopathy is a condition in which spinal nerves become irritated and cause radiating pain (16). Spinal spondylosis is a broad term for degenerative conditions related to pain caused by anatomical changes to vertebral bodies and intervertebral discs (17). Sacroiliac joint dysfunction is a condition in which the sacroiliac joint becomes inflamed and causes pain in the lower back (18). All of these conditions can result in chronic back pain that can be debilitating for patients. PRP therapy can be used as a treatment option for individuals with pain-related symptoms associated with these spinal conditions (1, 19). PRP therapy harnesses growth factors and cytokines associated with wound healing to target inflammation and tissue damage that results from degenerative spinal conditions. Studies have demonstrated that PRP therapy causes significant pain reduction and functional improvement in patients with chronic low back pain (19). Although the exact mechanism by which PRP therapy alleviates chronic low back pain is not completely understood, research suggests that the growth

factors and cytokines released by platelet alpha-granules play an important role in promoting wound healing processes like cellular proliferation, synthesis of proteins and angiogenesis (19, 20, 21).

# TENDINOPATHY

Tendinopathy describes a broad class of conditions in which tendons become inflamed and cause pain. The most common sites of inflammation are the elbow, rotator cuff, Achilles tendon and patellar tendon (22). Tendinopathies often result in prolonged healing times and symptom presentation because of the relatively minimal local blood flow to tendons. This hypovascular environment inhibits adequate and efficient healing of damaged tissue and leads to persistent inflammation and pain (22). PRP therapy can be used in treating tendinopathies to overcome the poor intrinsic healing ability of tendons. The cytokines and growth factors found in PRP can modulate multiple inflammatory processes, neovascularization and tissue remodeling to promote healing of damaged tendon tissue (22, 23). Studies have demonstrated that PRP therapy can provide clinically meaningful improvements in symptom relief for patients with tendinopathy (22, 24). Research also suggests that PRP therapy for tendinopathy may even enable biological healing of tissue injury, providing evidence that PRP therapy can stimulate innate healing mechanisms to promote tissue regeneration (25).

## ANDROGENETIC ALOPECIA

Androgenetic alopecia (AGA), commonly known as male-patterened baldness, is a disorder caused by hormonal and genetic factors that results in progressive hair loss (8). AGA pathogenesis is multifactorial, but the disorder results in the miniaturization of hair follicles. There are pharmacological interventions available to treat androgenetic alopecia, such as Minoxidil and Finasteride (26). These therapies are proven to be effective at stopping the progression of AGA but they also carry potential risk for adverse effects, such as skin irritation, hypertrichosis (excessive hair growth), erectile dysfunction, low libido, and depression (27, 28). PRP therapy has been demonstrated to be an effective alternative treatment for AGA. Studies have shown that PRP therapy can significantly improve hair density and thickness in patients with AGA without any major side effects (29, 30). According to current literature, PRP therapy may work as a treatment for AGA by providing growth factors to cells involved in the miniaturization of hair follicles (31). The growth factors provided by PRP therapy may play a key role in the maintenance of hair follicle integrity (30, 31).

### **SEXUAL HEALTH (ERECTILE DYSFUNCTION)**

Erectile dysfunction (ED) is the inability to achieve or maintain an erection sufficient for sexual performance. ED affects at least 12 million men in the United States and can be caused by myriad factors, including vascular, neurologic, psychological, and hormonal issues (32). A significant proportion of ED pathology is a result of endothelial dysfunction secondary to inflammation (33). Conventional treatments for ED include phosphodiesterase-5 inhibitors,

alprostadil, vacuum devices, and surgically implanted penile prosthetics (32). These traditional ED treatments stimulate the nitric oxide pathway to improve endothelial function. The nitric oxide pathway plays a major role in the initiation and maintenance of penile erections (34). Recent clinical and preclinical data has suggested that PRP therapy may be a safe and effective treatment for mild to moderate ED (35, 36). PRP therapy may improve erectile quality through the action of PRP growth factors in targeting inflammatory processes that may be dysregulated in ED patients (37).

# CONCLUSION

PRP therapy is a minimally-invasive treatment option for musculoskeletal conditions such as osteoarthritis, degenerative spinal conditions, tendinopathy, dermatological conditions like androgenetic alopecia and sexual dysfunction. The autologous nature of PRP therapy offers patients significant and long-lasting symptom relief with minimal risk of allergic or immune reactions. PRP therapy has immense potential for many clinical applications in pain management practices and represents an exciting progression in the field of regenerative medicine.

- Bhatia, Rohan, and Gaurav Chopra. "Efficacy of Platelet Rich Plasma via Lumbar Epidural Route in Chronic Prolapsed Intervertebral Disc Patients-A Pilot Study." Journal of clinical and diagnostic research : JCDR vol. 10,9 (2016): UC05-UC07. doi:10.7860/JCDR/2016/21863.8482
- 2. Redler, Lauren H et al. "Platelet-rich plasma therapy: a systematic literature review and evidence for clinical use." The Physician and sportsmedicine vol. 39,1 (2011): 42-51. doi:10.3810/psm.2011.02.1861
- Le, Adrian D K et al. "Current Clinical Recommendations for Use of Platelet-Rich Plasma." Current reviews in musculoskeletal medicine vol. 11,4 (2018): 624-634. doi:10.1007/s12178-018-9527-7
- Epifanova, Maya V et al. "Platelet-Rich Plasma Therapy for Male Sexual Dysfunction: Myth or Reality?." Sexual medicine reviews vol. 8,1 (2020): 106-113. doi:10.1016/j.sxmr.2019.02.002
- Poulios, Evangelos et al. "Platelet-Rich Plasma (PRP) Improves Erectile Function: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial." The journal of sexual medicine vol. 18,5 (2021): 926-935. doi:10.1016/j.jsxm.2021.03.008
- Singh, Jaspal Ricky et al. "The Effectiveness of Autologous Platelet-Rich Plasma for Osteoarthritis of the Hip: A Retrospective Analysis." Pain medicine (Malden, Mass.) vol. 20,8 (2019): 1611-1618. doi:10.1093/pm/pnz041
- Hohmann, Erik et al. "Is platelet-rich plasma effective for the treatment of knee osteoarthritis? A systematic review and meta-analysis of level 1 and 2 randomized controlled trials." European journal of orthopaedic surgery & traumatology : orthopedie traumatologie vol. 30,6 (2020): 955-967. doi:10.1007/s00590-020-02623-4
- 8. Stevens, J, and S Khetarpal. "Platelet-rich plasma for androgenetic alopecia: A review of the literature and proposed treatment protocol." International journal of women's dermatology vol. 5,1 46-51. 21 Sep. 2018, doi:10.1016/j.ijwd.2018.08.004
- 9. Dhillon, Robinder S et al. "Platelet-rich plasma therapy future or trend?." Arthritis research & therapy vol. 14,4 219. 8 Aug. 2012, doi:10.1186/ar3914
- Rai, Deepak et al. "Platelet-rich plasma as an effective biological therapy in early-stage knee osteoarthritis: One year follow up." SICOT-J vol. 7 (2021): 6. doi:10.1051/sicotj/2021003
- Pochini, Alberto de Castro et al. "Analysis of cytokine profile and growth factors in platelet-rich plasma obtained by open systems and commercial columns." Einstein (Sao Paulo, Brazil) vol. 14,3 (2016): 391-397. doi:10.1590/S1679-45082016AO3548
- 12. Amable, Paola Romina et al. "Platelet-rich plasma preparation for regenerative medicine: optimization and quantification of cytokines and growth factors." Stem cell research & therapy vol. 4,3 67. 7 Jun. 2013, doi:10.1186/scrt218
- Hunter, David J, and David T Felson. "Osteoarthritis." BMJ (Clinical research ed.) vol. 332,7542 (2006): 639-42. doi:10.1136/bmj.332.7542.639

- Shen, Longxiang et al. "The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials." Journal of orthopaedic surgery and research vol. 12,1 16. 23 Jan. 2017, doi:10.1186/s13018-017-0521-3
- 15. Waterman, Brian R et al. "Low back pain in the United States: incidence and risk factors for presentation in the emergency setting." The spine journal : official journal of the North American Spine Society vol. 12,1 (2012): 63-70. doi:10.1016/j.spinee.2011.09.002
- 16. Berry, James A et al. "A Review of Lumbar Radiculopathy, Diagnosis, and Treatment." Cureus vol. 11,10 e5934. 17 Oct. 2019, doi:10.7759/cureus.5934
- Middleton, Kimberley, and David E Fish. "Lumbar spondylosis: clinical presentation and treatment approaches." Current reviews in musculoskeletal medicine vol. 2,2 (2009): 94-104. doi:10.1007/s12178-009-9051-x
- Rashbaum, Ralph F et al. "Sacroiliac Joint Pain and Its Treatment." Clinical Spine Surgery vol. 29, 2 (2016): 42-48. doi: 10.1097/BSD.00000000000359
- Xu, Zhen et al. "Ultrasound-Guided Transforaminal Injections of Platelet-Rich Plasma Compared with Steroid in Lumbar Disc Herniation: A Prospective, Randomized, Controlled Study." Neural plasticity vol. 2021 5558138. 27 May. 2021, doi:10.1155/2021/5558138
- 20. Wu, Peter I-Kung et al. "Platelet-Rich Plasma." Physical medicine and rehabilitation clinics of North America vol. 27,4 (2016): 825-853. doi:10.1016/j.pmr.2016.06.002
- Anitua, Eduardo et al. "Autologous platelets as a source of proteins for healing and tissue regeneration." Thrombosis and haemostasis vol. 91,1 (2004): 4-15. doi:10.1160/TH03-07-0440
- 22. Miller, Larry E et al. "Efficacy of platelet-rich plasma injections for symptomatic tendinopathy: systematic review and meta-analysis of randomised injection-controlled trials." BMJ open sport & exercise medicine vol. 3,1 e000237. 6 Nov. 2017, doi:10.1136/bmjsem-2017-000237
- 23. Molloy, Timothy et al. "The roles of growth factors in tendon and ligament healing." Sports medicine (Auckland, N.Z.) vol. 33,5 (2003): 381-94. doi:10.2165/00007256-200333050-00004
- 24. Dragoo, Jason L et al. "Platelet-rich plasma as a treatment for patellar tendinopathy: a double-blind, randomized controlled trial." The American journal of sports medicine vol. 42,3 (2014): 610-8. doi:10.1177/0363546513518416
- 25. Gautam, V K et al. "Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: clinical and ultrasonographic evaluation." Journal of orthopaedic surgery (Hong Kong) vol. 23,1 (2015): 1-5. doi:10.1177/230949901502300101
- 26. York, Katherine et al. "A review of the treatment of male pattern hair loss." Expert opinion on pharmacotherapy vol. 21,5 (2020): 603-612. doi:10.1080/14656566.2020.1721463

- 27. Badri T, Nessel TA, Kumar D D. Minoxidil. [Updated 2021 Apr 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482378/
- 28. Irwig, Michael S. "Persistent Sexual and Nonsexual Adverse Effects of Finasteride in Younger Men." Sexual medicine reviews vol. 2,1 (2014): 24-35. doi:10.1002/smrj.19
- 29. Gentile, Pietro, and Simone Garcovich. "Systematic Review of Platelet-Rich Plasma Use in Androgenetic Alopecia Compared with Minoxidil®, Finasteride®, and Adult Stem Cell-Based Therapy." International journal of molecular sciences vol. 21,8 2702. 13 Apr. 2020, doi:10.3390/ijms21082702
- 30. Alves, Rubina, and Ramon Grimalt. "Randomized Placebo-Controlled, Double-Blind, Half-Head Study to Assess the Efficacy of Platelet-Rich Plasma on the Treatment of Androgenetic Alopecia." Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.] vol. 42,4 (2016): 491-7. doi:10.1097/DSS.00000000000665
- 31. Garg, Suruchi, and Shweta Manchanda. "Platelet-rich plasma-an 'Elixir' for treatment of alopecia: personal experience on 117 patients with review of literature." Stem cell investigation vol. 4 64. 18 Jul. 2017, doi:10.21037/sci.2017.06.07
- 32. Rew, Karl T, and Joel J Heidelbaugh. "Erectile Dysfunction." American family physician vol. 94,10 (2016): 820-827.
- 33. Vlachopoulos, Charalambos et al. "Unfavourable endothelial and inflammatory state in erectile dysfunction patients with or without coronary artery disease." European heart journal vol. 27,22 (2006): 2640-8. doi:10.1093/eurheartj/ehl341
- 34. Campbell, Jeffrey D, and Arthur L Burnett. "Neuroprotective and Nerve Regenerative Approaches for Treatment of Erectile Dysfunction after Cavernous Nerve Injury." International journal of molecular sciences vol. 18,8 1794. 18 Aug. 2017, doi:10.3390/ijms18081794
- 35. Poulios, Evangelos et al. "Platelet-Rich Plasma (PRP) Improves Erectile Function: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial." The journal of sexual medicine vol. 18,5 (2021): 926-935. doi:10.1016/j.jsxm.2021.03.008
- 36. Epifanova, Maya V et al. "Platelet-Rich Plasma Therapy for Male Sexual Dysfunction: Myth or Reality?." Sexual medicine reviews vol. 8,1 (2020): 106-113. doi:10.1016/j.sxmr.2019.02.002
- 37. Britt, Deron et al. "Availability of platelet-rich plasma for treatment of erectile dysfunction and associated costs and efficacy: A review of current publications and Canadian data." Canadian Urological Association journal = Journal de l'Association des urologues du Canada vol. 15,6 (2021): 202-206. doi:10.5489/cuaj.6947