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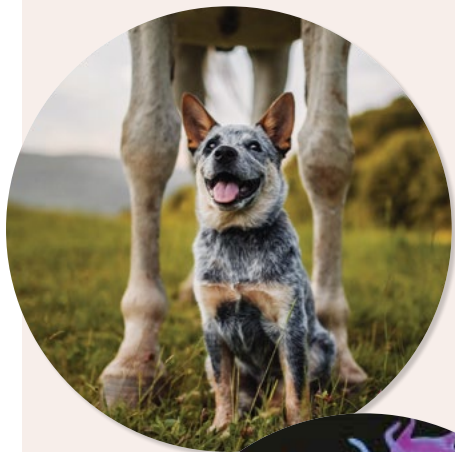
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8



11



18

Contents

4 Platelet-Rich Plasma: The Importance of Uniformity and Consistency

By Anne S. Hale, DVM

8 PRP Therapeutics: Common Indications and Dosing

By Anne S. Hale, DVM

11 Veterinary Allogeneic Platelet-Rich Plasma: Safety Overview

By Robert Harman, DVM, MPVM, and Anne S. Hale, DVM

14 Platelet-Rich Plasma and Stem Cells: How Biologics Work Together

By Anne S. Hale, DVM and Robert Harman, DVM, MPVM

18 Regenerative Medicine and the Veterinary Technician: A Quick Guide to PRP and Stem Cell Therapy

By Ashley Lentini, RVT and Robert Harman, DVM, MPVM

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Platelet-Rich Plasma: The Importance of Uniformity and Consistency

By Anne S. Hale, DVM

As we adjust our practices to accommodate a focus on providing for all ages and stages of our patient's lives, many veterinarians have been including cellular therapy to promote healing and pain control without a polypharmacy approach. There are several cellular therapies on the market with various claims relating to osteoarthritis control, wound healing, and pain control. Platelet-rich plasma (PRP) is one such biologic that has been utilized for decades to promote healing in acute and chronic soft tissue injuries, joint disease, corneal ulcers, chronic wounds, and more. Both large and small animals have benefitted from the presence of platelets during the healing process.

The Healing Properties of Platelet-Rich Plasma

Platelet-rich plasma is one of the most common biologics used in intra-articular, intralesional, and topical administration to assist with wound healing as well as inflammation and pain control. The goal is to deliver a concentrated dose of platelets to accelerate lagging internal healing processes by amplifying the biological signals that would naturally occur when platelets aggregate at a site of injury. In vitro and ex vivo testing of platelets as a part of the "cell healing team" suggests that PRP works due to the presence of platelet membrane interaction with damaged endothelium. This interaction leads to the expulsion of platelet alpha granules which are "packets" of growth factors and anti-inflammatory cytokines. These growth factors and cytokines signal to mesenchymal stem cells, macrophages, and T cells, which coordinate the healing process in the

immediate region. Platelet alpha granules routinely carry platelet-derived growth factor (PDGF-BB), vascular endothelial growth factor (VEGF), and CXCL12 (potent stem cell recruiter). In all, over 200 proteins have been identified in the granules that are associated with angiogenesis, wound healing, coagulation, and endothelial repair.

Platelets are anuclear organelles that have a limited lifespan of usually not more than 1-3 days when activated. When used as a biologic, PRP should have a suitable amount of alpha granule content available for action in that period of time. This translates to total platelet dose. Higher concentrations of platelets (>3X baseline) are recommended for intralesional and intra-articular treatment protocols based on published clinical trials. In the review of thirty papers published in the last ten years, a dosing structure of 3 to 8 times baseline has been associated with positive outcomes after administration of PRP.^{1,2}

Platelet-Rich Plasma Production

Commonly, autologous PRP is produced from the patient's whole blood using a mechanical device (kit) involving centrifugation to separate platelets and white cells from the rest of the whole blood. Typically, the mechanical device uses a proprietary tube often paired with a filtering gel or mechanism to segregate the platelets and plasma from whole blood. The purpose of these devices is directed towards platelet collection and concentration along with plasma. Leucocytes may or may not be included in the collection process depending on which system is used. Ideally, PRP should have minimal hemoglobin and red blood cell contamination as this can cause transfusion-like adverse events and antibody formation. Autologous PRP devices do not require FDA index or review before marketing.

FIGURE 1

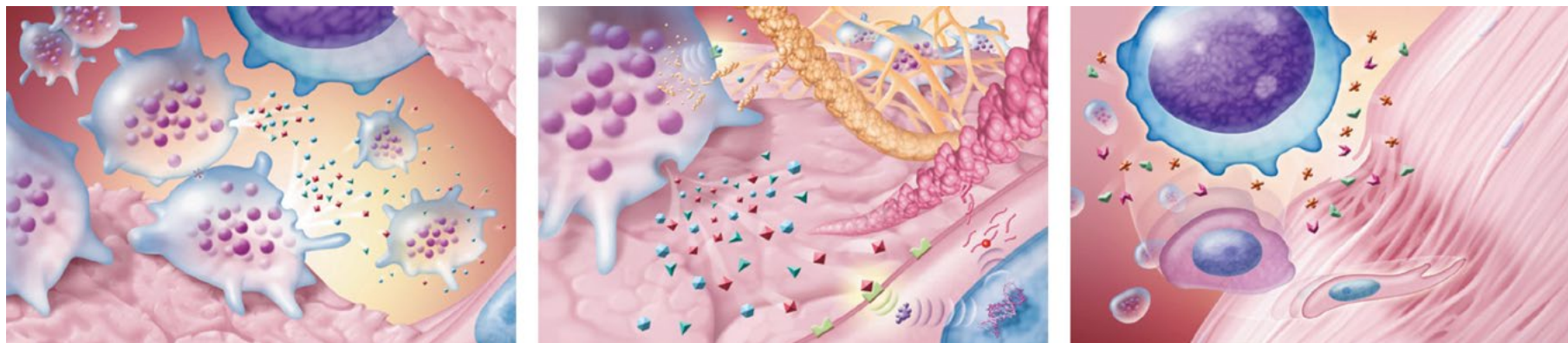


Diagram of general platelet activation and action. (A) Platelets are stimulated by an agonist such as thrombin at a vascular tear or inflammation. (B) Granule membranes fuse with the platelet plasma membrane, releasing the chemical messengers to the platelet exterior. (C) Platelet cytokines call mesenchymal stem cells and leucocytes in to orchestrate the repair.

Variability in Platelet-Rich Plasma Products

Autologous PRP has the advantage of minimizing the potential for transfusion reaction on administration of the product because the recipient donates their own blood for processing. However, autologous PRP production has several disadvantages that can impact the outcome in your patient's response to therapy. Most commonly, autologous PRP production is negatively influenced by the inflammatory state of the patient, platelet count of the patient, operator handling of the sample, and the effectiveness of the PRP mechanism (kit) used to produce the product. This variability of the injectable product can lead to inconsistent or ineffectual treatment.

In a recent comparison of four PRP kits for the production of equine PRP, these kits demonstrated a lack of uniformity relating to the final platelet

count and platelet concentration (Table 1). Variability was noted despite utilizing the same operator, centrifuge, and platelet counter. Outcomes, as indicated by platelet count in the PRP, were also variable. Additionally, each kit failed to meet their respective platelet concentration claim.

Allogeneic “Off-The-Shelf” Platelet-Rich Plasma

Platelet count directly correlates to the amount of growth factors and anti-inflammatory cytokines available for treating the joint, soft tissue lesion, or surface wound. Variability in therapeutic outcomes can occur when the product is not uniform, especially relating to platelet concentration and total platelet dose. The results above show wide variation between actual platelet concentration and that claimed by the PRP mechanical device manufacturer.

TABLE 1				
PRP Mechanical	Platelet Count FINAL (platelets/ μ L)	Leucocyte Count (Leucocytes/ μ L)	Tested Platelet Concentration from Baseline	Company Claim: Platelet Concentration
Gel Test 1	387,000/ μ L	1,900/ μ L	2X	7X
Gel Test 2	367,000/ μ L	27,000/ μ L	3X	7X
Gel Test 3	213,000/ μ L	1,700/ μ L	1.5X	9X
Tube Test 2	450,000/ μ L	Not performed	6X	9X

Comparison of four PRP mechanicals currently available today. Equine cells from random equine donors were drawn for comparison of these tests. All tests were performed to manufacturer standards using an experienced phlebotomist.

“ PRP represents an affordable cellular therapy to offer your patient as an aid to healing through cell signaling to regenerative cells, control of inflammation, and the promotion of cell growth.”

Newer generation allogeneic products like PrecisePRP™ avoid this variation by pooling donors and confirming the characteristics of the PRP during manufacture. This uniformity leads to a more consistent patient response to the cellular therapy and is advantageous in older or more

diseased patients whose autologous PRP production is negatively influenced by the inflammatory state of the patient.

Conclusion

PRP represents an affordable cellular therapy to offer your patient as an aid to healing through cell signaling to regenerative cells, control of inflammation, and the promotion of cell growth. A consistent and repeatable product, like any pharmaceutical, is key to the best patient outcomes. ●

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PLAY



PRP Therapeutics: Common Indications and Dosing

By Anne S. Hale, DVM

Today, the veterinary practitioner has many product choices for regenerative medicine. It is important to understand how and why these products work in the area of interest to maximize your patient's opportunity for success. Biologics, including cell-based products, are available both as an autologous and allogeneic formulation. A review of how cells, specifically platelets, work to promote injury repair and inflammation resolution is necessary to support the correct use of platelet-rich plasma.

What is PRP and How Can it be Used?

By definition, platelet-rich plasma (PRP) is a concentrated platelet product with native plasma. The purpose for platelet concentration is to provide a higher number of platelets than you would find in normal blood circulation in an effort to enhance local angiogenesis, regulate cellular activity, home stem cells, proliferate stem cells, and deposit matrix proteins to support healing and regeneration of tissue.¹

Published uses of PRP in the dog and horse include repair and regeneration of muscle, ligament, tendon, bone, dermis, epidermis, and cornea. Most commonly, veterinary clinicians have experience with PRP and its uses for musculoskeletal diseases and injuries.² Its use in large wounds and burns has also been well documented. Corneal ulceration, keratoconjunctivitis sicca, and descemetocoele are frequent ophthalmic uses of PRP. Historically, surgeons have placed PRP at the site of fracture repair to enhance healing post-surgery. More recently, PRP has been utilized intra-cavitary to address inflammation,

for example endometritis or chronic cystitis. The veterinary practitioner has long since seen these treatment modalities as a way to “home” stem cells.

Recognizing the broader role that the platelet plays in endothelial stabilization and hemostasis, PRP has also been explored in laminitis, sepsis, hemorrhagic shock, and traumatic brain injuries. Each of these disease indications rely on the platelet to support an anti-inflammatory environment while participating locally in the stabilization of the local hemostatic environment.

Largely through topical or intra-articular applications, PRP has been used to provide local analgesia and sourcing for growth factors. In addition, these applications have supported an antibacterial role for the PRP through its ability to signal other cell types.

Factors Supporting Successful PRP Therapy

Successful PRP therapy is based on total platelet dose, the functionality of the platelet membrane, and ability to degranulate. Published reviews and clinical studies utilizing autologous PRP produced by a medical device show that variability in platelet number, platelet activity, and platelet phenotype lead to variable clinical outcomes.

Allogeneic pooled platelet-rich plasma offers an opportunity to overcome these concerns by providing a consistent platelet number, minimizing premature activation and degranulation, as well as controlling donor variability. Once this variability has been overcome, then successful PRP therapeutics are based on an overconcentration of platelets in the lesion, joint, or topical location. A review of PRP therapy and clinical outcomes written by Carmago Garbin et al. supports that five times the normal circulating platelet count is ideal for positive outcomes.³

PRP Dosing Considerations

Dosing PRP requires an understanding of the disease indication as well as the location. For instance, if the area to be treated is a synovial membrane and the subintimal connective tissue layer, then PRP should be dosed for maximum effect to allow for “bathing” of the cavity and penetration into the subintimal layer. Intra-articular administration allows for delivery to the lesion without dependency on intravascular circulation as well as local concentration of product. Published human reports on intra-articular use of PRP suggests that approximately 2.5 billion platelets are needed to provide the appropriate total platelet dose for positive outcomes.⁴

When treating intralesional defects, dosing is affected by the size of the lesion as well as its location and time from injury. These lesions, such as superficial digital flexor tendon tears or supraspinatus tendinopathies, may be treated with a similar total platelet dose. Published randomized trials in equine patients with superficial digital flexor tendinopathies support a total platelet dose of 2.7 billion platelets divided into three sites with positive outcomes.⁵

Topical dosing must be calculated depending on the lesion size, containment in the lesion, and activation level of the platelets. This type of use is focused on exposing the lesion to high quantities of growth factors to promote regeneration and angiogenesis. Strategies for maintaining contact in these areas include adding fibrin, synthetic gels, and/or topical creams to “hold” the platelets in the area until degranulation. Specifically, corneal ulceration therapeutics involve subconjunctival injections of PRP once weekly for two to three treatments. In a study of 28 dogs/cats, subconjunctival injections were successful in promoting resolution in corneal ulceration when given two to three times at a frequency of once weekly.⁶

Common Uses of Platelet-Rich Plasma in Veterinary Medicine

Wound Healing

Musculoskeletal Disease/Injury

- Osteoarthritis
- Tendon/Ligament Tear
- Muscle Injury

Post Surgical Healing

Dental and Oral Surgical Procedures

Ophthalmic Uses

- Corneal Ulceration
- Keratoconjunctivitis Sicca
- Descemetocoele

In Conjunction with Stem Cell Therapy



“ Allogeneic PRP has the advantage of being an off-the-shelf therapeutic with a known and consistent platelet dose and potency. ”



Conclusion

In studies where the platelet count can be controlled and site administration is localized, positive outcomes with the use of PRP can be expected. Allogeneic PRP has the advantage of being an off-the-shelf therapeutic with a known and consistent platelet dose and potency. This provides an easy and convenient way to administer PRP therapy to your patients for a variety of disease indications. ●

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Veterinary Allogeneic Platelet-Rich Plasma: Safety Overview

By Robert Harman, DVM, MPVM, and Anne S. Hale, DVM

Platelet-rich plasma (PRP) has been studied in multiple species with varying use profiles. A thorough review of the platelet-rich plasma literature yielded over 30 references in support of PRP and its use as a topical, intra-articular, and/or intralesional therapy published since 2008. Meta-analysis in human clinical trials as well as multiple study reviews in canine and equine suggest that the most common concern for platelet-rich plasma effectiveness is associated with a lack of uniformity and standardization.^{1,2} Important components of platelet-rich plasma have been debated; however, total platelet dose, growth factor content, and leucocyte count appear to be common factors for most authors when relating in vitro characterization and effectiveness outcomes.³

Platelets are provided to supply the growth factors and cytokines predominately located in the alpha granules. After administration, the growth factors and cytokines are released into the area of injection and provide anti-inflammatory cytokines and repair signaling. Platelets also release factors that attract or “home” mesenchymal stem cells, leucocytes, and other mononuclear immune cells to assist in the repair process. It has been reported that PRP injected into the joint or lesion reduces pain signaling.

In using the commonly available PRP produced by mechanical device, the safety issues include sterility, variability in dose, contamination with unwanted cell types (white and red blood cells) and variability in potency. This has led to interest in providing the benefits of PRP from a more standardized and quality controlled PRP derived from allogeneic donors.⁴ To facilitate convenience of delivery and use, lyophilization can be employed

to deliver a room-temperature stable and readily used form of PRP. Manipulating the storage parameters for platelet concentrates prior to pooling and lyophilization allows platelet lyophilization without cryopreservatives (VetStem data, 2022, 2023)

Platelet Therapy-Definition

The most common term for platelet therapy is “platelet-rich plasma.” The term platelet-rich has been used loosely to describe solutions where the platelet concentration is higher than that found in whole blood and the platelets are suspended in plasma. The growth factors stored in the alpha granules in platelets⁵ are most often cited as the active healing agents including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-β), and basic fibroblast growth factor (bFGF).⁶

The most common method to concentrate platelets is centrifuge spinning. As stated by Dr. Sam Franklin (2016, Veterinary Practice News), most of the systems on the market are designed for preparing human platelet concentrates and are sold into the veterinary markets without published data supporting suitability for veterinary species. In a search for published data on methods and clinical results, one may be surprised to find most systems have only testimonial data.

Allogeneic Donor-derived PRP Manufacturing Standards

PrecisePRP™ Equine is a leucoreduced allogeneic, pooled freeze-dried, platelet-rich plasma product from up to 18 equine donors and is used here as an example of a donor-derived PRP product. The biological source material for this product is in-date leucoreduced,



apheresis-derived equine platelet concentrates and apheresis-derived frozen plasma. All horses are blood type AaCa positive and negative for plasma antibodies directed at blood types they are not. Donors are from a closed herd compliant with USDA regulations for production of licensed biologics. Selection of donors as well as evaluation or vaccination for infectious disease is compliant with FDA CVM Guidance #254. Supplied in a 50 mL glass vial, this product is a sterile, nonpyrogenic white-to-tan powder. Once rehydrated with 8mL of sterile water for injection, this product is a gold translucent fluid with 4.0×10^9 platelets per vial, less than 1500 white blood cells per μL , and less than 0.01% red blood cells.

PrecisePRP™ Canine is a leucoreduced allogeneic, pooled, freeze-dried, platelet-rich plasma product from up to 32 canine donors. The biological source material for this product is in-date leucoreduced, apheresis- derived canine platelet concentrates and apheresis-derived or whole blood-derived frozen plasma. Donors are blood typed for DEA 1, 4, and 7 as well as tested for plasma antibody negative to routine canine red blood cell antigens. Selection of donors and evaluation for infectious disease is compliant with FDA CVM Guidance #254. Supplied in a 50 mL glass vial, this product is a sterile, nonpyrogenic white-to-tan powder.

Once rehydrated with 8mL of sterile water for injection, this product is a light yellow translucent fluid with 4.0×10^9 platelets per vial, less than 1500 white blood cells per μL , and less than 0.01% red blood cells.

PrecisePRP™ Randomized Controlled Safety Study in the Equine

VetStem, Inc. sponsored the conduct of an equine safety study at request of FDA with a primary objective to evaluate the safety of leucoreduced equine allogeneic pooled freeze-dried platelet rich plasma (PRP, PrecisePRP™ Equine) for intra-articular injection in adult horses.

Precise PRP™ Equine was studied, at the request of FDA Center for Veterinary Medicine, in a randomized, masked, placebo-controlled target animal safety study (adult horses) .The study design was intraarticular injection at the label dose of 4 mL in comparison to a blinded control group injected with 4 mL of placebo saline. This study was conducted with a formal IACUC approval and was conducted at an independent

veterinary school testing facility. The horses were injected in one radio carpal joint and one tarsocrural joint, with the injections being two weeks apart. Horses were followed for seven days after each injection and monitored for clinical and laboratory safety of the PrecisePRP™ Equine injections.

There were no treatment-related adverse reactions reported. The study included evaluations of daily health, temperature, pulse, respiration, clinical pathology, injection sites reactions (heat, swelling, passive flexion pain and joint circumference), veterinary physical exams, and lameness evaluations (including evaluation by a clinician and by the Lameness Locator® system). A single adverse event in the placebo group was reported as colic, which resolved within one day. The adverse event table below shows that four control horses and one treated horse had mild transient lameness attributed to the needle injection procedure.

ADVERSE EVENT	PRECISEPRP™ EQUINE (N=6)	SALINE PLACEBO (N=6)
Mild transient lameness post-injection	1	4
Colic	0	1

This study of the safety of the intraarticular administration of PrecisePRP™ Equine demonstrated a good margin of safety at the label dose of 4 mL. There were small excursions from normal ranges for some measurements, but no clinically significant excursions or trends were detected.

PrecisePRP™ Randomized Controlled Safety Study in the Canine

PrecisePRP™ Canine was studied in a randomized, masked, placebo-controlled safety study in adult beagles at request of the FDA. Design was intra-articular injection at the label dose of 2 mL in comparison to a blinded control group injected with 2 mL of placebo saline. The dogs were injected in one stifle joint and one hip joint, with the injections being two weeks apart. Dogs were followed for seven days after each injection and monitored for clinical and laboratory safety of the PrecisePRP™ Canine injections. This study was conducted with a formal IACUC approval and was conducted at an independent testing facility.

There were no adverse treatment-related effects on body weights, gait, daily health observations, temperature, pulse, respiration, clinical pathology, injection sites, no

significant findings on veterinary physical exams, and no adverse events because of treatment. Specific evaluations of the injected joints included heat, joint swelling, and passive flexion pain as well as lameness evaluation.

Literature Review of Safety of Allogeneic PRP

Published safety data exists for both canine and equine allogeneic platelet-rich plasma. Clinical case reports, systemic literature reviews, preclinical safety analysis, and comparative studies with autologous platelet-rich plasma and mesenchymal stem cells are available for the horse and dog. In the safety evaluation published by Garbin⁴, a pooled allogeneic freeze-dried PRP was evaluated with autologous frozen products for safety and found to be statistically unremarkable from autologous products relating to inflammation and lameness post injection. In an Italian clinical trial in canine patients, no adverse events associated with immunogenicity were noted utilizing a pooled allogeneic platelet-rich plasma⁷.

In addition, there are safety articles on the use of allogeneic PRP in the human. In a 2021 review of the literature, Akbarzadeh found 2 laboratory animal studies and 8 human studies of allogeneic PRP safety in wound healing⁸. The authors concluded “none of the studies identified any major side effects or adverse events” and “the treatment resulted in a reduced time to heal and/or reduced wound size in most cases.” In a 2023 human meta-analysis of autologous PRP, as a reference for PRP efficacy and safety in osteoarthritis, the authors included 24 randomized controlled trials comprising 1,344 patients⁹. Their conclusion stated that PRP injection therapy can safely and effectively improve functional activity in patients with osteoarthritis (OA) and produce positive analgesic effects in patients with knee OA, temporomandibular joint OA, and ankle OA. In addition, they found that the analgesic effect of leucocyte-poor PRP was greater than that of leucocyte-rich PRP.

Conclusions

Based upon the literature and the randomized, masked, placebo-controlled safety studies cited above, allogeneic PRP presents a low safety risk and may be advantageous in comparison to mechanical PRP kits. Allogeneic PRP provides an off-the-shelf solution with a known and consistent platelet dose and significantly reduces the safety issues and dose variability associated with mechanically produced PRP. ●

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For a complete reference list, email info@vetstem.com.

Platelet-Rich Plasma and Stem Cells: How Biologics Work Together

By Anne S. Hale, DVM and Robert Harman, DVM, MPVM

Introduction

Platelet-rich plasma (PRP) is used commonly in canine and equine practice. A very common question is if there is any advantage of combining PRP with a stem cell product. Recent scientific publications demonstrate that not only is it possible, but the combination has a synergistic effect compared to each product individually. Clearly, they have different mechanisms of action as seen in Table 1, but let's explore how they work in synergy.

Mechanisms of Action

Platelets are provided to supply the growth factors and cytokines predominately located in the alpha granules. After administration, the growth factors and cytokines are released into the area of injection and provide anti-inflammatory cytokines and repair signaling. Platelets also release factors that attract or “home” mesenchymal stem cells, leucocytes, and other mononuclear immune cells to assist in the repair process. It has been reported that PRP injected into the joint or lesion reduces pain signaling.

Mesenchymal stem cells (MSC), on the other hand, are tissue/injury responsive drug stores that manufacture and release injury specific drugs to promote healing, reduce inflammation, modulate the immune system, and reduce pain. Additionally, they are directly antibacterial and antiviral.

PRP and Stem Cells Work Synergistically

PRP is immediately available naturally any time there is an injury, and the stem cell synergy assists the body in providing all the necessary components to treat an injury and

promote healing. As you can see from Table 1, these key natural components provide complementary and supportive functions.

In a hallmark study of osteoarthritis in beagle dogs, PRP combined with adipose derived stem cells was superior to either therapy alone and better than placebo controls.¹ These benefits were evident in lameness score, compressive strength of the cartilage, COL and GAG content of cartilage, as well as a reduction in cartilage content of proinflammatory cytokines like TNF- α , IL-1 α , and COX2. The author's conclusion was “taken together, this study shows that the combination of MSC and PRP has a beneficial and synergistic effect on OA via the ECM synthesis and chondrocyte proliferation and via the anti-inflammatory reaction.”

In a recent review publication, models of periodontal disease, tendon repair strength, osteoarthritis, bone repair, skin and soft tissue repair, and in cardiovascular disease demonstrated that the combination of PRP and MSC was superior to the individual components alone.² The same synergy was demonstrated in a rat spinal cord injury model where the authors concluded “this study showed that combination of MSCs and PRP synergistically promotes their therapeutic effects in the SCI (spinal cord injury).”³

Case Report

A 15-month-old Clydesdale gelding presented for regenerative care to resolve a large, post-surgical wound. After routine castration, bacterial infection, and surgical debridement, a 9cm x 3cm x 11cm surgical wound extending from the internal inguinal ring to the surface of the prepuce was open and draining serosanguinous discharge (Figure 1). The horse was discharged to home care which included daily cleaning with hypertonic saline and topical application of silver/manuka honey. At recheck after one week at home, the wound was clean but still substantial.

Expected timeline for healing was discussed at 4 months. To speed healing and slow the serosanguinous discharge, cellular biologic therapy was discussed.

The owner had banked stem cells at the time of castration with VetStem, Inc. for later orthobiologic care. This meant that stem cells were immediately available for use. In addition, the allogeneic PRP, PrecisePRP™ Equine, was available for use. PrecisePRP™ Equine is currently under final review with the FDA ACTP program. Based on the availability of these two biologics, a treatment plan was developed.

Stem cells were administered intravenously for the anti-inflammatory effect and potentiation of healing. PRP was administered topically by rehydration of the allogeneic PrecisePRP™ Equine and syringe flushing of 8mls PRP (4 billion platelets) into the deep aspects of the wound. The wound was packed with sterile gauze for 4 hours to allow the PRP to absorb into the wound tissue and release growth factors like PDGF-BB and VEGF to promote angiogenesis. In addition, the PRP releases high mobility group box 1 (HMGB1) which works to mobilize MSC as a chemoattractant.⁴

Daily care was continued with the inclusion of repeat PRP administration, as described above, two weeks after the initial use and MSC administration. Wound size and health were evaluated weekly. On week 5, the wound was assessed as 7cm x 1/2cm x 3cm with healthy granulation tissue present without serosanguinous discharge. By week 6, the wound was completely closed (Figure 2) and the gelding returned to normal turnout during week 6. He was placed back in training on week 8 with no further complications noted. Although this use of PrecisePRP™ Equine is off-label, wound healing is a very commonly reported application.

Conclusions

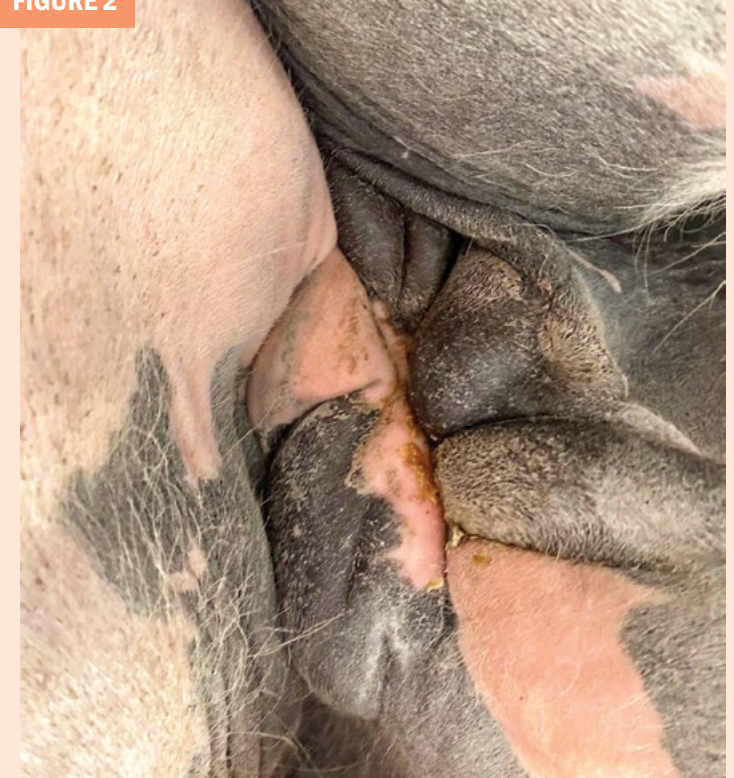
Based upon the literature, PRP and stem cells are strongly synergistic. There are complementary mechanisms of action that work together to improve healing and tissue repair in many different organs/tissues across multiple species. ●

“ PRP and stem cells are strongly synergistic. There are complementary mechanisms of action that work together to improve healing and tissue repair in many different organs/tissues.”

TABLE 1

Mechanism of Action (Characteristic)	PRP	Stem Cell
Responsive cell with nucleus that can replicate		X
Can produce specific cytokines in response to injury type		X
Can deliver cytokines and growth factors	X	X
Can attract mesenchymal stem cells to a site of injury	X	
Modulate the immune system		X
Antibacterial	X	X
Antiviral	X	X
Hemostatic	X	
Stimulate wound healing	X	X
Reduce pain	X	X
Anti-inflammatory	X	X

Comparison of mechanisms of action of PRP and mesenchymal stem cells

FIGURE 1**FIGURE 2**

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PLAY



Regenerative Medicine and the Veterinary Technician: A Quick Guide to PRP and Stem Cell Therapy

By Ashley Lentini, RVT and Robert Harman, DVM, MPVM

Veterinary technicians often serve as the first and last point of contact with pet owners. They are charged with fielding and answering questions and are typically a wealth of knowledge when it comes to various treatment options. Regenerative medicine is an innovative field in veterinary medicine that shows great promise for patients. For this reason, veterinary technicians will benefit from learning the basics of two of the most common regenerative medical treatments: platelet-rich plasma (PRP) and stem cell therapy.

The goal of regenerative medicine is to assist the body in regenerating tissue damaged by disease or injury. Every day, veterinary technicians encounter patients with fractures, soft tissue injuries, and joint disease. Traditional treatments include cage rest, medications, physical therapy, or in some cases, surgery. PRP and stem cells offer additional options for pain management and healing.¹ These two therapies can be used separately or in combination to achieve a synergistic effect.

A Brief Overview of Platelet-Rich Plasma

Platelets are the body's first responders to injury and inflammation. Platelets release alpha granules at the site of injury or inflammation. Alpha granules contain both growth

factors and cytokines. Growth factors promote the creation of new, healthy tissue while cytokines have anti-inflammatory properties.² Utilizing PRP amplifies the body's own healing capacity and can also act as a homing beacon for stem cells, which further promote healing.

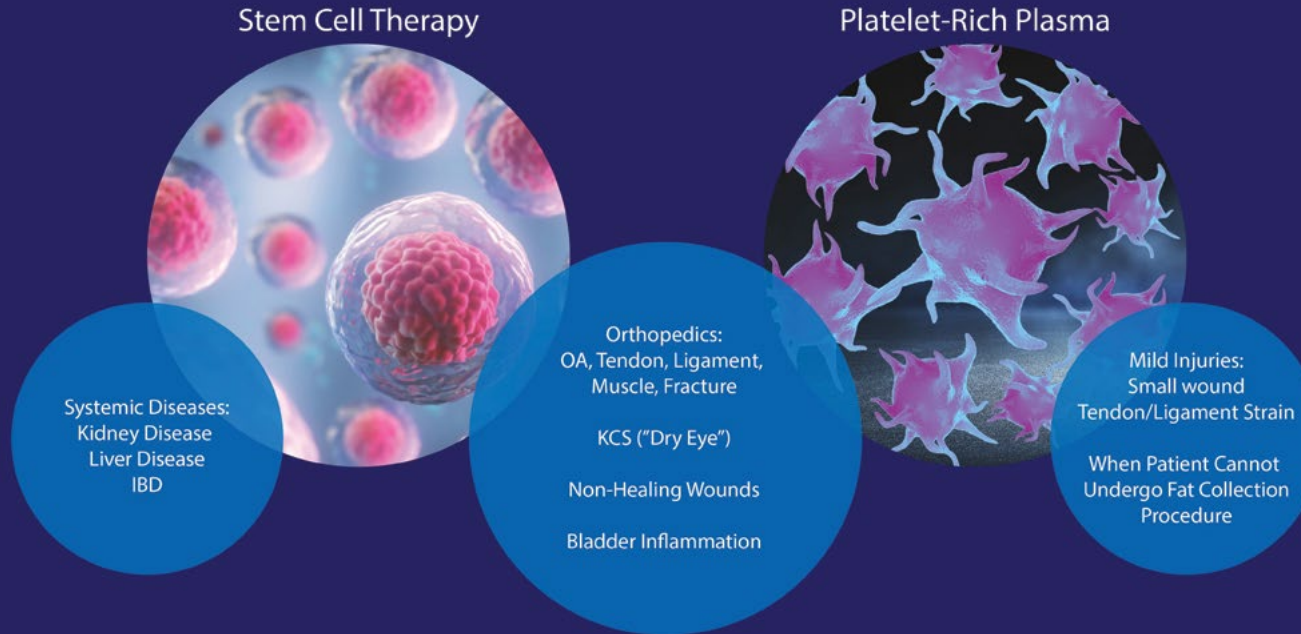
The Basics of Stem Cell Therapy

Stem cells are derived from a variety of sources: embryonic, bone marrow, and adipose tissue. Adipose derived stem cells are the most accessible cells for the average veterinary clinic.³ Stem cells stimulate regeneration in bone, joint, tendon, and ligament injuries. Stem cells also act as drug factories churning out potent biomolecules to reduce inflammation and pain. In immune-mediated diseases, stem cells will buffer or modulate an overactive immune system to reduce the attack of the body on itself. Stem cells can home to areas of injury and inflammation to begin reducing that inflammation and working to heal damaged tissue.

Common Uses of PRP and Stem Cell Therapy

Many of the conditions veterinary technicians see weekly can benefit from regenerative medical treatments. Orthopedic indications are the most common use of PRP and stem cell therapy. Osteoarthritis has become one of the biggest concerns in veterinary medicine

When to Use Stem Cell Therapy and Platelet-Rich Plasma (PRP)



Use Stem Cell Therapy and PRP together to Achieve Synergistic Effect

because patients are living longer, and their owners have become more adept at recognizing pain in their pets. Owners are also looking for alternatives to traditional drugs to control pain and inflammation in their pets while reducing the side effects. Both PRP and stem cells are very useful in the treatment of orthopedic conditions but utilizing them together can provide a more profound outcome.

Outside of orthopedics, there are many uses for both PRP and stem cell therapy being studied and tested in clinical trials. Both PRP and stem cells

can be used in conditions such as dry eye (KCS),⁴ non-healing wounds,⁵ and even bladder inflammation.⁶ PRP is not indicated for systemic conditions that would require intravenous administration. Stem cells can be delivered IV and are therefore a potential therapy for conditions such as inflammatory bowel disease and kidney disease. Conversely, there are cases where PRP might be more appropriate such as for milder injuries (small wounds, tendon/ligament strains) or in patients who cannot undergo the surgical fat collection required to harvest stem cells.

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How is PRP Prepared

Until recently, the method of obtaining PRP required a kit, a centrifuge, and plenty of technician time and expertise. PRP kits on the market currently require approximately 10-60 mLs of whole blood. The blood draw needs to be an extremely clean “stick” to get the largest number of platelets for treatment and to avoid contamination of the blood collected. These kits require centrifuging at specific speeds for a specified amount of time and careful handling after centrifuging to preserve the injectable product.

The downsides to autologous (patient derived) PRP from these kits are worth mentioning. The most obvious is that the amount of blood is prohibitive to some of the smaller or geriatric patients in clinics. It is also dependent on the patient’s production of platelets. If the patient has lower than normal platelets, which can occur for a variety of reasons, their PRP will have fewer platelets as well. Ensuring that the blood collection is done without any clotting, and that the centrifuge is properly calibrated and set for the correct spin time and RPM are also crucial to the preparation of the final injectable product. Each of the above indicated issues can cause lower than optimal platelet counts, and that variability in the number of platelets in PRP can affect the efficacy of treatment. Many clinics do not have a platelet counter that can properly measure the higher concentration of platelets to even know the delivered dose.

Donor Derived PRP Can Help Mitigate These Shortcomings

New to the market is a product that resolves many of these concerns. PrecisePRP™ is a shelf stable allogeneic (donor derived) PRP product. This product is species specific for both dogs and horses and is currently in its final phase of FDA review. PrecisePRP™ is room temperature stable and easily reconstituted with sterile water, a process that veterinary technicians are familiar with and perform multiple times a day. This product can be used on patients of all sizes since there is no blood draw required. Platelet count and potency is known on each vial, meaning a consistent and therapeutic dose of platelets can be delivered with each injection of PrecisePRP™. The best thing about this product for the veterinary technician is that it doesn’t take them off the clinic floor for 20-30 minutes to prepare.

Stem Cell Processing in an FDA Compliant Facility

Stem cell therapy has a similar dichotomy: there are countertop machines made to process stem cells in the hospital as well as companies that process adipose tissue and create doses using FDA compliant methods and standardized equipment in FDA compliant facilities. The latter option is much more accessible for most clinics as it does not require training or a large capital investment, or use of counter space. Like off the shelf PRP, using the processing laboratory saves technician time and keeps them on the floor to perform other tasks.

The VetStem cell processing lab has the added benefits of utilizing an extremely accurate cell counter that ensures a therapeutic dose of stem cells,⁷ much like PrecisePRP™ for platelets. Frozen storage of additional doses as well as culturing for more doses are all handled at the lab, taking the burden off veterinary staff, and providing reassurance to the owner that their pet can receive future treatments with their own stem cells if needed.

Conclusion

Veterinary technicians are a key respected source of information for clients. Having up to date knowledge on the latest therapies allows technicians to better educate clients. Regenerative medicine is now easily



available through PrecisePRP™ and VetStem and technicians can be at the forefront of advocating for their patients and moving their clinics forward. This knowledge allows technicians to easily present the case for regenerative medicine to veterinarians and clients alike. VetStem offers RACE approved CE courses for technicians and veterinarians seeking more in-depth knowledge. ●

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