Regenerative Medicine - Part Two: PLATELET-RICH PLASMA AND EXTRA-CELLULAR MATRIX

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In the last article about regenerative techniques, we discussed the use of stem cells in the horse. This month, the series on regenerative medicine continues with a short discussion on Platelet-Rich Plasma (PRP) and Extra-cellular Matrix ("scaffolding").

When a tendon or ligament is injured there is initially a certain degree of hemorrhage, which then incites an inflammatory response. This is seen immediately with lameness, heat, pain on palpation and swelling. Following this, the body then 'cleans up' the injured site by removing dead tissue cells and debris. At this point, when the tendon or ligament is imaged with the ultrasound a hole or "core lesion" can be seen. It is into this that a regenerative treatment (stem cells, PRP, or ECM) can be injected.

PRP actually first became popular for use in human patients for treatment of wounds, for bone healing, and for blood clotting. This has been adapted for use in the equine patient in recent years. You may also have seen this referred to as Autologous Conditioned Serum (ACS). This refers to the fact that the 'product' is derived from the horse's own body (blood), which then reduces the potential for a reaction or "rejection". When it proved to be successful in filling in human bone defects, other uses were sought, and there was a cross over to adapt its use to the equine patient.

Platelets are a component of blood and are responsible for clot formation during injury. A loss of integrity in a structure (due to injury) stimulates platelets to 'work' and aid in the initiation of repair of that structure. As they migrate to and reach the site of the injured tissue, they release a number of vital products as well as stimulate other cells in the vicinity to release theirs.

This effect is called "trophism" and may be a vital factor in the promotion of wound healing. The products released include growth factors, stimulating factors for local mesenchymal stem cell production, and anti-inflammatory mediators. Working with each other, begin forming a matrix within the injured tissue. Injecting PRP into a tendon or ligament lesion has increased the probability of producing the 'correct' collagen that composes the tendon or ligament fibers. This then reduces the amount of fibrous or scar tissue formation within the healing tendon and thus optimizes the repair and potentially reduces the probability of re-injury.

How do we "get" the platelets? Under sterile conditions, a small volume of blood is taken from the jugular of the injured horse. The blood is then placed into special vials that are placed into a centrifuge. High-speed centrifugation causes the platelets to remain in a separate layer from the other cells in the blood. They are then drawn up into a syringe for injection. Again, using sterile technique the PRP is injected into the injured tendon or ligament using ultrasound guidance. The process takes approximately 1 hour from blood draw to being injected into the horse, and can be done as an outpatient procedure.

PRP can also be formed into a gel for application onto skin wounds to promote healing. In tendons and ligaments, it can be used in acute as well as chronic lesions. It can be used alone or in combination with stem cells and followed up with shockwave treatments, usually starting 10-14 days after injection, to optimize the response. Simultaneous injection of stem cells and PRP maximizes the probability of cell migration to and differentiation at the injured site.

The use of Extra-cellular Matrix (ECM) is not a new technique and has been available to equine practitioners for a number of years. It was primarily used in the treatment of injuries to the suspensory ligament and has also been

used for the treatment of large wounds. Normal cells in the body need to be anchored to ECM to survive that is, they cannot survive if they just 'float' around in a disorganized manner. The mechanism by which this ECM works, is to provide the cells that are migrating to the injured site for repair a "scaffold" upon which they can congregate and fill in the defect. ECM also provides a signaling mechanism that stimulates local stem cells to proliferate and repair damaged tissue such as in a ligament or tendon defect. There are two major sources of ECM; that derived from small intestine, and the other from urinary bladder (A-Cell). The ECM has no cells associated with it and is indeed the 'skeleton' upon which a tissue gains its structure. Because it is 'acellular', there is less likelihood that there would be an immune response (rejection) when it is injected into the horse. This product has been used for many problems in human and veterinary medicine including in treatment of large defects in corneas as well as soft tissue injuries and skin wounds.

The ECM product comes in two forms: a powdered form that is used for injection into the injured tendon or ligament, or as a sheet that can be laid directly onto a wound. As with the other techniques, this is done as a sterile procedure in a controlled environment. Injection into suspensory ligaments has been done for a number of years. There has reportedly been some local reactions, swelling, and heat immediately after injection. This is thought to be a result of the stimulation of local cells by the ECM to move to the defect and proliferate. The reaction resolves quite quickly with symptomatic therapy.

Again, as with the stem cells, the ultrasonographic appearance of 'healing' after the use of PRP and ECM can occur quite rapidly. But the appropriate time for recovery must be given to the horse as the repaired lesion must mature and gain strength so that it is not injured again and this does take several months.

All of these regenerative techniques are novel and do not have many years of scientific research to support or refute their use in the horse. The literature

that has been published from research studies and case studies to date has been promising. From personal use of these modalities, the impression of this author is that there is improved healing and a superior ultrasonographic appearance of the injured tendon or ligament after using a regenerative treatment.

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