Regenerative Medicine: A Practicing Surgeon's Perspective on the Use of Regenerative Medical Techniques in the Sport Horse

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“Regenerative medicine” refers to treatments that restore or help heal adult body parts. There are three main strategies for the repair of these adult body parts:

- Stem cells or progenitor cells
- The induction of regeneration by chemical substances such as hormones, growth factors, scaffolds, medications, or other signaling mechanisms
- The transplantation of in vitro grown organ and tissues.

Currently in equine medicine and surgery, the first two mechanisms have been most commonly utilized. Little research has been published on the use of in vitro derived organs and tissues for use in the equine patient. Much attention has been focused on the use of “stem cells” for the augmentation of healing and more recently the use of augmented products such as platelet rich plasma, growth factors and scaffolds. The purpose of this presentation is to discuss the current state of these treatments in the equine athlete.

Most of the current uses of regenerative medicine in the horse have focused on the healing of tendon, ligament, and cartilage injuries. The major issue with tendon and ligament injuries is not that these structures do not heal, it is that they heal with a vast amount of scar tissue which is invariably inferior to the original tissue, resulting in a high recurrence rate of re-injury. By augmenting the healing process with various techniques, the hope is that a more physiologically stable tissue will replace the normal weaker scar tissue. Therefore the ideal treatment should aim to avoid the formation of excessive fibrous tissue and regenerate normal tendon matrix.

Four separate components have been suggested to be required for an ideal healing approach. While each can be used independently, all four in conjunction would likely provide the best results. They include the following:

- Appropriate mechanical environment
- Scaffold
- Anabolic stimulus
- Cell source

The mechanical environment would be the matrix in which the healing occurs. Typically a scaffold system is utilized to support the cells and extracellular matrix in such a way as proper alignment and healing can occur. Currently two products have been utilized as a scaffold. The first is ACELL Vet an intra-lesional treatment for tendon and ligament injuries that comes from porcine urinary bladder. The other is autogenous derived bone marrow injection.

ACell Vet is suggested to provide both a scaffold as well as growth factors that attract endogenous mesenchymal stem cells. It has been associated with significant inflammatory reactions after injection and while there are copious anecdotal reports of its benefits, there is little objective data published on its efficacy.

Autogenous bone marrow injection is purported to provide a scaffold in the form of fibrin within a core lesion of a tendon or ligament injury. Included with the bone marrow are a very small number of autogenous stem cells, growth factors, and hormones that may benefit in the healing process as well. Few side effects are noted from these injections and since it is derived autogenously, reactions are rare. Scientific publications are few for bone marrow injections.

Growth factors such as insulin-like growth factor 1 (IGF-1) and equine recombinant growth hormone (rEGH), have shown promise in research settings but have little long-term follow up available in a clinical setting.

Platelet rich plasma (PRP) is becoming much more common for treating tendon and ligament injuries. PRP generally has an increased platelet count compared to that of whole blood and can be prepared by either centrifugation or filtration. PRP contains TGF-B1, IGF-1 and platelet derived growth factor (PDGF) within the platelets of the product and all are anabolic stimuli for cell growth.
Mesenchymal stem cells have the most promising potential effects as they can possibly differentiate into a variety of tissues. However, this may not be their primary mode of action. Embryonic stem cells have been reported to be pluripotent and are of great interest in human medicine. Embryonic stem cells have the risks of being allogeneic and have the risk of teratoma formation and are not currently readily available for use in horses.

Post-natal stem cells are classified into hematopoietic and mesenchymal stem cells. The latter is the cell lineage of interest since they have the potential to develop into a variety of musculoskeletal tissues. Since these cells can be harvested from adult tissue and used in the same patient, they are not allogenic and no immune response is created in the autogenous implantation process. There are two main regions of mesenchymal stem cell retrieval currently, bone marrow cultured MSC’s and fat-derived cultured or processed (adipose derived stromal fraction) MSC’s. Both have some basic research showing their improvement in the laboratory setting and both have data to support their improvement in a clinical setting, although much of this research is in its infancy.

In conclusion, the use of regenerative medicine techniques is in its infancy, and will no doubt continue to evolve quickly as more is learned about the intricacies of the healing process.

I. REFERENCES