

# Regenerative Medicine – Understanding IRAP, PRP and Stem Cell Therapies

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Several advanced scientific therapies for previously untreatable joint disease and equine injuries have been introduced into equine veterinary medicine over the last decade. Veterinarians use IRAP, PRP and stem cell therapies to manipulate the body's biological mechanisms to stimulate healing.

There is ongoing research for these therapies and new information is gathered each day. While the promise of cure is very exciting for both veterinary professionals and horse owners, it is important for the owner to understand the science behind each therapy in order to have a reasonable expectation for success.

## **IRAP**

IRAP stands for Interleukin-1 Receptor Antagonist Protein and recently is being referred to as autologous conditioned serum. Equine athletes are susceptible to musculoskeletal injuries and osteoarthritis or degenerative joint disease. Osteoarthritis is a common cause of lameness in horses. Clinical signs include lameness, joint swelling and inflammation. These signs are a result of cartilage damage within the joint and inflammation of the joint lining or synovitis. Joint trauma results in the release of inflammatory mediators such as IL-1 and other cytokines. These cytokines including IL-1 can lead to further cartilage damage causing a vicious cycle of cartilage and joint damage which result in joint inflammation and lameness.

IRAP was developed to counteract IL-1 that is produced in the traumatized joint and to slow the progression of osteoarthritis. IRAP works by preventing IL-1 binding to the IL-1 receptors in the joint therefore blocking the damage and inflammation caused by IL-1.

IRAP involves drawing approximately 50 mls of your horse's blood into a specialized syringe which stimulates the production of the antagonist protein. The blood is incubated in the syringe for 24 hours. After incubation the blood is placed in a centrifuge and the plasma which is rich in the antagonist protein is separated from the blood cells in multiple syringes. IRAP is then injected into the joint once every 7-10 days for 3-5 treatments. Samples are stored in a -80 C freezer until use.

There are currently two products on the market - IRAP and IRAP II. IRAP is from Dechra Pharmaceuticals and IRAP II is from Arthrex Vet Systems. Recent research has compared the 2 products and concluded that IRAP II has a modestly improved cytokine profile but both products produced a significant

increase in interleukin-1 receptor antagonist. These 2 products have not been compared clinically to determine if there is a clinically significant difference between the 2 products.

### **Platelet Rich Plasma (PRP)**

PRP is another product that is derived from your horse's own blood. Platelets are loaded with numerous growth factors that are released upon platelet activation. Large amounts of transforming growth factor beta (TGF- $\beta$ ) and platelet derived growth factor and smaller amounts of insulin-like growth (IGF), epidermal growth factor (EGF) and TGF- $\alpha$  are released upon activation. These growth factors and others act synergistically to enhance access of healthy inflammatory cells to the area of tissue injury, formation of new blood vessels (angiogenesis), formation of new connective tissue (fibroplasia) and regeneration of skin (re-epithelialization).

PRP can be obtained in a matter of minutes. There are currently a variety of PRP kits available. Usually a centrifuge is used to help concentrate the platelets into the plasma which then can be used for treatment. PRP has been most commonly used to treat tendon and ligament injuries. The goal of treatment is to accelerate and improve the quality of healing. Recently veterinarians have begun to use PRP intra-articular to treat osteoarthritis.

### **Stem Cell Therapy**

Stem cell therapy is an exciting new area of treatment for equine injuries. Although there is much we still need to learn, early research is very encouraging. Current ongoing research will begin to offer answers and to shed some light on the best applications and techniques for the use of stem cell therapy.

Stem cells are undifferentiated cells that have the ability to replicate and differentiate into a diverse range of cell types. These cell types include tendon, ligament, cartilage, muscle and bone. There are two basic types of stem cells, hematopoietic and mesenchymal. We are primarily concerned with mesenchymal stem cells (MSC) because they appear to have the best potential for regenerative medicine. These MSC are found in bone marrow, fat, umbilical cord blood and tissue, and many other organs throughout the body. The younger or more immature the stem cell, the more potential they may have. The younger stem cells have an increased ability to heal and regenerate tissue compared to the adult stem cells. This is the reason for the recent interest in storing umbilical cord blood in horses.

In equine practice stem cells are commonly derived from bone marrow obtained from the sternum or the tuber coxae. Once the bone marrow has been obtained it is sent to a lab where it is cultured and expanded into millions of stem cells. The

typical dose ranges from 10 to 25 million stem cells per treatment. The culture and expansion process takes approximately 3-4 weeks. The stem cells can then be injected into the affected tendon, ligament or joint. Recently, we have also been using stem cells to treat chronic laminitis cases with encouraging results. The multiple uses for stem cells have yet to be determined.

The second source of stem cells is fat. Fat derived stem cells only contain 2-4% stem cells unless they are cultured and expanded. Therefore adipose derived stromal fraction is the more appropriate term used to describe this therapy.

Research comparing bone marrow derived to fat derived stem cells indicate that bone marrow derived stem cells are superior to fat derived stem cells.

IRAP, PRP and stem cell therapies offer the possibility of successful treatment of previously life-threatening or career-ending injuries. Consult your veterinarian to determine if one of these treatments may be appropriate for your horse.

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