

## Interleukin-1 Receptor Antagonist Protein (IRAP®) Therapy for Equine Osteoarthritis Amanda M. House, DVM, DACVIM and Alison Morton, DVM, MSpVM, DACVS

A novel therapy called IRAP®, Interleukin-1 Receptor Antagonist Protein, is now available and showing promising results for the treatment of osteoarthritis in horses. Equine athletes are susceptible to musculoskeletal injuries and osteoarthritis (OA), also known as degenerative joint disease (DJD). Osteoarthritis has a major economic impact on the horse industry and dictates the level of performance for many horses and their riders. Conventional therapies for osteoarthritis include rest; nonsteroidal anti-inflammatory drugs (NSAIDs), such as bute, Banamine®, and Equioxx®; intraarticular (joint) injections with hyaluronic acid and/or corticosteroids; intramuscular Adequan®; intravenous Legend®; oral supplementation with products such as glucosamine and chondroitin sulfate, and extracorporeal shockwave therapy. IRAP® was originally developed in Europe and has been used extensively in Germany. It is being marketed in the United States by Arthrex VetSystems, and is recommended for the treatment of synovitis (inflammation of the joint lining) and mild to moderate OA.

Osteoarthritis is one of the most common causes of lameness in the horse. It is the result of multiple factors which can include conformation, age, type of performance, conditioning, trauma, development diseases, and multiple physiologic factors. The clinical signs of OA include lameness, poor performance, stiffness, and joint swelling and inflammation. These signs are a result of synovitis and progressive cartilage damage within the joint. Trauma (physical or chemical) to the joint surface results in the formation and release of inflammatory proteins, such as interleukin-1 (IL-1) and other cytokines, which result in cartilage degeneration. Cytokines, including IL-1, are chemical signals produced by cells in the immune system and tissues of joints, that may speed up joint injury and potentiate inflammation. Articular cartilage normally has a smooth surface and is a critical component of joint stability and fluid motion. It is also resilient and acts to absorb a great amount of force exerted through locomotion. Damage to the cartilage initiates a cycle of inflammation and pain, increased inflammatory protein production, and thus further cartilage degeneration. This process can become a vicious cycle if not treated and arrested in a timely fashion. Over time, bony changes will occur, which account for abnormalities commonly seen on radiographs ("x-rays") of joints with OA.

IRAP® was developed to counteract the inflammatory protein interleukin-1 that is produced in the joint during synovitis and to slow the progression of OA. It prevents IL-1 from binding to IL-1 receptors on tissues within the joint, and therefore blocks the action of and stops the damage caused by IL-1 in the joint. The IRAP procedure requires drawing about 50 ml of your horse's blood. The blood is collected and incubated for 24 hours in a special syringe which stimulates production of the antagonist protein. After incubation, the blood is placed in a centrifuge and the plasma (containing IRAP) is separated from the blood cells. The plasma is stored in multiple aliquots and placed in a special freezer at -80 degrees Celsius for use at any time. The IRAP-rich plasma is then thawed and sterilely injected into the affected joint. The joint is usually treated every 7-10 days for 3 or more treatments with 1-8 ml, depending on the size and location of the joint. Rest is typically recommended for at least 5-7 days following the injection, per your veterinarian.

Preliminary studies show that IRAP® is improving lameness and may decrease joint swelling. Horses likely to benefit most from IRAP® are those with synovitis or mild to

moderate OA or other conditions that may result in a secondary inflammation within a joint. IRAP® can not reverse any permanent damage that often exists in joints with OA, but may serve to prevent further inflammation and reduce progression of disease. It is likely that other therapeutics may also be needed in conjunction with IRAP® therapy to treat horses with OA. Some horses with severe osteoarthritis that were refractory to other therapies are reported to have improved with the addition of IRAP® therapy, however, IRAP® is generally not recommended for horses with severe cartilage loss. Talk to your veterinarian, as they are the best resource to determine if IRAP® is right for your horse.