The use of stem cells in clinical small animal cases is both controversial and full of potential. Protocols for the use of stem cells in clinical cases have been extrapolated from the equine literature without a large number of case controlled studies in small animals. The most common autogenous regenerative cells used in small animals are the bone marrow derived stem cells and the adipose derived regenerative cells. The focus of this talk will be on bone marrow derived stem cells and their orthopedic applications.

The exact mechanism of action of stem cells when injected into a ligament, tendon or joint is not known. We do know that mesenchymal stem cells will migrate to areas of inflammation within the body, are able to differentiate into different cells types, will secrete cytokines that suppress inflammation, and are able to modulate the immune system. Initially, it was thought that when mesenchymal stem cells were injected into a joint, they began forming new tissue, i.e. cartilage, however more recently there is evidence that suggests that the stem cells may act at the periphery of the joint allowing antiinflammatory mediators to enter in order to encourage repair at the site of injury.

Bone marrow derived stem cells are obtained via a bone marrow aspirate under heavy sedation or general anesthesia. Generally, 500U of heparin is placed into a 10cc syringe and approximately 3-5 ml of bone marrow is obtained. The most common sites for bone marrow aspiration are the ilial wing and proximal humerus. The author submits these samples to Advanced Regenerative Therapies in Fort Collins, Colorado for culture and expansion. Additional details on obtaining and shipping the sample to ART can be obtained from http://www.art4dvm.com/PDF/ART-Canine-Marrow-Aspiration-Protocol.pdf.

Generally, 2-3 weeks is necessary for culture and expansion of bone marrow derived stem cells. The cells arrive at the clinic or hospital cryopreserved and are resuspended immediately prior to injection. The optimal cellular dose for injection is unknown. However, most commonly there are 5 million cells per ml in samples injected by the author and generally each treated joint is injected with one ml of fluid. Certainly, aseptic technique is very important to reduce the risk of introducing an infection at the site of injection.

Uses for mesenchymal stem cells in small animal medicine include intraarticular injection after partial meniscectomy in the stifle and medial coronoidectomy in elbows with dysplasia. MSC injections are also used for palliative treatment of advanced osteoarthritis. Additionally, they can be used as a primary treatment for Achilles tendonitis or as a means of speeding the recovery with surgical repair.

There is a pilot study published in 2005 showing that dogs with induced meniscal tears treated with bone marrow had improved angiogenesis, chondrogenesis, prominent immune cell infiltrate and proliferation of the fibroblasts compared to untreated induced meniscal tears. Stifle joints were treated with whole bone marrow and isolated mononuclear cells from the bone marrow. There was complete healing in 6 of 8 menisci that were treated. There was complete healing in only 3 of 8 in the control group.

Another study reported at the Veterinary Orthopedic Society meeting March 2012 in Crested Butte evaluated dogs receiving stem cell injections in various joints for osteoarthritis at Veterinary Referral Center of Colorado between 2009 and 2011. There were 105 dogs treated and 25 had complete Hudson’s outcome data at 6 weeks and 6 months post injection(s). Dog
owners’ perception of pain (VAS score) was significantly improved at both 6 weeks and 6 months compared to preinjection scores.

The goat model has been used to show the effect of stem cells on induced osteoarthritis. These goats had their anterior cruciate ligament resected and their medial meniscus completely excised. In the treatment group, the goats received an intraarticular stifle injection of mesenchymal stem cells and hyaluronic acid; while the control group was only treated with hyaluronic acid. The treated group had evidence of medial meniscal regeneration. The treated group also had less articular cartilage degeneration, osteophytic remodeling, and subchondral sclerosis compared to the control group.

The equine model has provided evidence for stem cell treatment for ligamentous and tendinous injuries. Typically, soft tissue injuries in the horse are career ending. In one study of horses with soft tissue injury treated with stem cells, one-half of the horses were able to return to or exceed their previous work levels. This model has been used for treatment of Achilles injuries in dogs.

Specific case examples of dogs with meniscal injury, osteoarthritis and soft tissue injury treated with mesenchymal stem cells will be presented.

References

- Devitt C. Clinical experience with stem cells at VRCC. VOS Presentation 2012.