



Stem Cell Therapy in Veterinary Orthopaedics: From Laboratory Research to Clinical Practice

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Orthopaedic disorders such as osteoarthritis, tendon and ligament injuries, cartilage defects, delayed fracture healing, and musculoskeletal trauma are important causes of pain, lameness, and reduced productivity in animals. Conventional treatments, including surgery, immobilization, physiotherapy, and anti-inflammatory medication, remain essential; however, complete restoration of damaged tissues is not always possible. Stem cell therapy has emerged as a promising approach in regenerative veterinary medicine because certain cells can influence inflammation, support tissue repair, and release biologically active molecules. Mesenchymal stromal cells (MSCs), obtained from sources such as adipose tissue, bone marrow, and umbilical tissues, have received particular attention in canine and equine orthopaedics. Clinical studies have investigated their use in osteoarthritis and tendon injuries, while applications in bone regeneration and cartilage engineering continue to develop. Nevertheless, outcomes vary according to the cell source, manufacturing process, administration method, disease severity, and rehabilitation protocol. This article discusses the biological basis, laboratory preparation, clinical applications, limitations, and future prospects of stem cell therapy in veterinary orthopaedics.

Keywords: Stem cells, mesenchymal stromal cells, veterinary orthopaedics, regenerative medicine, osteoarthritis, tendon injury, tissue engineering.

Introduction

Orthopaedic diseases are encountered frequently in small and large animal practice. Dogs may develop osteoarthritis, cranial cruciate ligament-associated joint disease, and fractures, whereas horses commonly suffer from tendon and ligament injuries that interfere with athletic performance. In cattle and buffaloes, fractures and limb injuries can cause prolonged recumbency, reduced productivity, and substantial economic losses. Traditional orthopaedic treatment aims to restore anatomical alignment, provide mechanical stability, control pain, and promote functional recovery. Nevertheless, some tissues, particularly articular cartilage, have limited intrinsic healing capacity. Tendons and ligaments may also heal through scar formation, which does not always reproduce the original tissue's mechanical properties. Regenerative medicine aims to improve tissue repair by using biological materials, cells, and tissue-engineering strategies. Stem cell therapy is one component of this field. It has attracted attention because stem cells and related stromal cells can interact with immune cells, influence inflammatory responses, and release growth factors and other signalling molecules involved in tissue repair. However, stem cell therapy should not be regarded as a universal replacement for conventional surgery. Its clinical value depends on the condition being treated, the quality of supporting evidence, and appropriate case selection.

Understanding Stem Cells and Mesenchymal Stromal Cells

Stem cells are characterized by their ability to self-renew and, depending on their type, differentiate into specialized cells. Adult mesenchymal stromal cells are widely investigated

in veterinary regenerative medicine because they can be isolated from several tissues and expanded under controlled laboratory conditions. The term mesenchymal stromal cells is often preferred when the full criteria for defining stem cells have not been demonstrated. These cells are generally studied for their capacity to support tissue repair through multiple biological mechanisms.

Common sources of MSCs

Adipose-derived MSCs: These cells are isolated from fat tissue. Adipose tissue is often accessible during elective surgery and can provide a useful starting material for cell isolation and expansion.

Bone marrow-derived MSCs: Bone marrow, commonly collected from selected skeletal sites, contains stromal progenitor cells. Bone marrow-derived preparations have been investigated in musculoskeletal repair, including tendon and joint disorders.

Umbilical cord and other perinatal tissues: Umbilical cord, Wharton's jelly, and related tissues are investigated as potential sources of cells with regenerative properties. Their use requires appropriate donor screening, collection, and manufacturing procedures.

The choice of cell source depends on availability, intended clinical application, processing requirements, cost, and the evidence supporting its use.

How Does Stem Cell Therapy Work

The therapeutic effects of MSCs are complex. Although these cells can differentiate into certain tissue-related cell types under appropriate experimental conditions, their benefits in living patients are not explained solely by direct replacement of damaged cells.

Immunomodulation

MSCs can release signalling molecules that influence the activity of immune cells. Depending on the local environment, these signals may help regulate excessive inflammation and create conditions more favourable for tissue repair. These effects are variable and should not be interpreted as universal suppression of inflammation.

Paracrine signalling

MSCs release growth factors, cytokines, extracellular vesicles, and other bioactive substances. These products may influence resident cells, blood-vessel formation, cell survival, and tissue remodelling. Such paracrine effects are considered important mechanisms of MSC-based therapies.

Support for tissue repair

In laboratory models, MSCs may demonstrate the ability to differentiate towards bone-forming or cartilage-related lineages under appropriate conditions. However, differentiation observed in culture does not guarantee that transplanted cells will form mature, functional tissue inside an animal.

Interaction with the tissue environment

The success of cell therapy also depends on the surrounding extracellular matrix, blood supply, inflammatory environment, mechanical loading, and rehabilitation. A damaged joint or tendon provides a different biological environment from a healthy laboratory culture.

Consequently, cell-based treatment is best understood as a potential means of influencing the body's repair response rather than a simple process of replacing damaged tissue with new cells.

From Laboratory Research to Clinical Application

The development of a cell-based therapy requires several carefully controlled stages.

Stage 1: Cell collection: Adipose tissue or bone marrow is collected from an appropriate donor or patient using a suitable aseptic procedure and veterinary oversight. The collection method depends on the species, tissue source, and intended application.

Stage 2: Cell isolation and culture: The collected tissue is processed using a validated method to obtain the desired cell population. Cells may be expanded in a laboratory using an appropriate culture medium and controlled environmental conditions.

Laboratory culture requires strict attention to aseptic technique, contamination prevention, cell identity, and consistency between batches.

Stage 3: Characterization and quality control: Before a cell preparation is considered suitable for administration, its relevant quality attributes should be assessed. These may include cell identity, viability, sterility, donor eligibility, and other tests appropriate to the product and intended use. Where relevant, functional potency assays may help determine whether the cells demonstrate the biological activity expected of the preparation.

Stage 4: Preparation for clinical use: The cell preparation is handled and formulated according to a validated protocol. The route of administration may be intra-articular, intralesional, or another route appropriate to the indication. The choice of route, dose, and formulation should be supported by evidence for the particular product and condition.

Stage 5: Clinical monitoring: Treatment outcomes should be assessed using predefined measures, such as lameness scores, pain assessment, joint range of motion, functional performance, imaging findings, and adverse-event monitoring. Follow-up is necessary to determine whether improvements are sustained.

Importantly, a successful laboratory experiment does not establish clinical efficacy. Translation into practice requires well-designed studies in animals with naturally occurring disease, appropriate comparison groups, and meaningful clinical outcomes.

Clinical Applications in Veterinary Orthopaedics

Osteoarthritis in dogs and horses

Osteoarthritis is a chronic joint disorder characterized by changes in articular cartilage, subchondral bone, synovium, and other joint tissues. It can cause pain, stiffness, reduced mobility, and impaired quality of life. MSC-based treatments have been investigated as potential adjuncts to conventional osteoarthritis management. Proposed benefits include modulation of joint inflammation and support for a healthier joint environment. Clinical studies in dogs and horses have reported encouraging results in selected cases, but outcomes are not uniform across products and study designs. Symptomatic improvement should not automatically be interpreted as regeneration of normal articular cartilage or reversal of established osteoarthritis. Stem cell therapy should therefore be considered within a comprehensive management plan that may include weight control, controlled exercise, rehabilitation, analgesia, and other evidence-based treatments.

Tendon and ligament injuries in horses

Tendon and ligament injuries are important causes of lameness in athletic horses. The superficial digital flexor tendon is particularly vulnerable to injury because it experiences substantial mechanical loading during locomotion. Healing commonly involves the formation of fibrous repair tissue. Although this tissue restores continuity, its organization and mechanical properties may differ from those of the original tendon, potentially increasing the risk of reinjury. Equine MSC research has investigated whether cell-based treatments can influence tendon repair and improve the quality of healing. Clinical studies have explored the use of bone marrow-derived and other MSC preparations in tendon injuries. This is one of the more established areas of investigation in veterinary regenerative medicine, although the strength of evidence differs among products and protocols. Appropriate diagnosis, controlled rehabilitation, and gradual return to exercise remain essential components of treatment.

Cartilage defects

Articular cartilage has limited intrinsic repair capacity because it lacks a direct blood supply and contains relatively few resident cells. Focal cartilage defects can therefore remain difficult to manage. Researchers have investigated MSCs, biomaterial scaffolds, and tissue-engineering strategies to support cartilage repair. In experimental systems, cells may be combined with hydrogels or other biomaterials to create a supportive environment. Nevertheless, producing durable, well-integrated cartilage that withstands normal joint loading remains challenging. The use of MSCs for cartilage regeneration should not be presented as a routine, universally proven treatment for naturally occurring cartilage defects.

Fracture healing and bone defects

Fracture repair depends primarily on adequate blood supply, biological viability, mechanical stability, and appropriate alignment. Most uncomplicated fractures do not require stem cell therapy; conventional fracture stabilization remains the foundation of treatment. Cell-based approaches are being investigated for difficult situations, including critical-sized bone defects, delayed union, and non-union. MSCs may be combined with osteoconductive biomaterials, extracellular matrix scaffolds, or other tissue-engineering constructs. A scaffold can provide structural support and a surface for cell attachment, while the cells and their secreted factors may influence the local repair response. However, promising results from experimental models cannot be assumed to translate directly into routine clinical success. In large animals, the substantial forces acting on the limb make mechanical stabilization especially important. A biological treatment cannot compensate for an unstable fracture fixation construct.

Tissue Engineering: Combining Cells with Scaffolds

One important direction in regenerative orthopaedics is the combination of cells with biomaterials. Tissue engineering integrates cells, scaffolds, and biological signals to support the formation or repair of tissue. Potential scaffold materials include collagen, hydrogels, decellularized extracellular matrix, and other biocompatible materials. An extracellular matrix scaffold may provide structural components and biological cues that influence cell attachment, migration, and behaviour. For example, a decellularized nerve or other tissue-derived matrix may be investigated as a supportive environment for cells in experimental tissue-repair models. The scaffold must be assessed for residual cellular material, structural integrity, biocompatibility, and appropriate processing. The same principle applies to bone and cartilage repair: the scaffold must be suited to the mechanical and biological requirements of the target tissue. A material that works well in a laboratory culture may not withstand the forces present in a weight-bearing limb. Cell-scaffold combinations are promising research tools, but their clinical use requires evidence of safety, manufacturing consistency, and meaningful improvement over existing treatment options.

Safety, Limitations, and Practical Challenges

Despite growing interest in veterinary regenerative medicine, several limitations remain. Variable treatment outcomes: Differences in donor characteristics, cell sources, processing methods, dose, viability, route of administration, and disease severity can influence results. Manufacturing quality: Contamination, inconsistent cell characteristics, inadequate storage, and handling errors can compromise a cell product.

Incomplete evidence: Many applications are supported primarily by experimental research, small clinical studies, case series, or studies using different outcome measures. These limitations make it difficult to compare results and identify the most effective treatment protocol.

Cost and accessibility: Cell collection, laboratory processing, quality control, transportation, and follow-up may increase treatment costs and limit access in some veterinary settings.

Safety monitoring: Potential concerns include infection, inflammatory reactions, unwanted tissue responses, and complications related to the collection or administration procedure. The nature and magnitude of these risks depend on the product and clinical application.

Regulatory requirements: Cell-based veterinary products may be subject to regulatory requirements that vary by country and product classification. In the United States, the Food and Drug Administration states that animal cell and tissue products intended to treat disease or affect body function generally fall under its regulatory framework. Its public guidance also emphasizes that promising scientific results must be supported by well-designed studies before clinical benefits can be established.

For these reasons, veterinarians should critically evaluate the evidence, avoid unsupported claims, explain uncertainties to animal owners, and follow applicable regulations.

Future Perspectives

Future progress will depend on improving cell characterization, potency testing, manufacturing consistency, and clinical trial design. Research is also examining extracellular vesicles, cell-free products, biomaterial scaffolds, and personalized approaches to regenerative treatment. A major priority is the development of standardized outcome measures that allow meaningful comparisons between studies. Long-term follow-up, transparent reporting of adverse events, and comparisons with established treatments will be essential. In veterinary orthopaedics, the most useful therapies are likely to be those that integrate biological repair with sound surgical principles, mechanical stabilization, pain management, and rehabilitation.

Conclusion

Stem cell therapy represents an important area of development in veterinary regenerative medicine. MSCs may influence inflammation and tissue repair through a combination of signalling, immunomodulatory, and context-dependent differentiation mechanisms. Research in canine osteoarthritis and equine tendon injuries has produced encouraging findings, while applications in cartilage regeneration, difficult bone defects, and scaffold-based tissue engineering remain areas of continuing investigation. The transition from laboratory research to reliable clinical treatment requires rigorous quality control, appropriate case selection, controlled clinical studies, long-term monitoring, and compliance with regulatory requirements. Stem cell therapy should be regarded as a developing component of veterinary orthopaedics, used alongside established treatment principles rather than as a replacement for them.