Strategies for the Treatment of Tendon and Intra-Articular Injuries

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Decades of research on tendon and ligament injuries have yielded extensive knowledge of the mechanical and biological properties of these dense connective tissues, translating into advances in surgical and conservative therapies that can prevent injury recurrence and prolonged lameness in horses. However, tendon and ligament injuries remain a persistent clinical challenge. Here, we will review management principles of soft tissue injuries focusing primarily on tendinitis.

Tendon injury is a common and debilitating musculoskeletal health problem in equine athletes. Re-injury rates vary from 12.5 to 53% in different equestrian disciplines, with the most common issues arising in racing athletes. Flexor tendons often exceed the physiological limit for strain during exercise, resulting in partial and complete tears accompanied by inflammation are not uncommon. High intensity exercise and aging dramatically increase the risk of injury. Scar tissue formation, characterized by poor fiber cross-linking and suboptimal biomechanical properties, is believed to be responsible for the high incidence of re-injury.

Tendons are made up of tendon fibrils, which consist of long bundles of collagen filaments. **Type I collagen** makes up the majority of the fibrils. Type I collagen has a larger diameter fiber and is stronger, in comparison to the smaller type III and Type V collagen found in tendons. Elastin and various glycoaminoglycans makes up the extracellular matrix. Tendon fibers are collected together to make up fascicles which can move independently from each other during tendon stretching. Ligaments have more irregular fiber pattern and can have remnant muscle cells with the ligament. Perfusion of the tendon comes from longitudinal vessels and vessels penetrating from the peritendinous tissue through the connective tissue around the tendon called the paratenon. Longitudinal vessels, which course the length of the tendon, anastomose with the transverse vessels. There are few penetrating vessels seen in tendons contained within the tendon sheath making these regions relatively avascular.

Biomechanically, tendons have a linear Stress-Strain relationship. Once loaded the relation between stress and strain in the tendon becomes linear or as load (stress) is applied to the tendon there is an equivalent lengthening (strain) of the tendon. As the tendon reaches the end of its ability to stretch (compliance) the fibers undergo plastic deformity and stretch beyond their capacity to return to normal length. Repeated loading of the normal tendon as in training a horse for exercise, increases fiber size similar to hypertrophy of muscle fibers that are exposed to increased load.

Signs characteristic of tendinitis (traumatic tendon injury) include
- lameness,
- swelling
- increased heat
- pain on palpation

After severe tendon injury where plastic deformity has occurred, the first sign is lameness due to loss of support of the tendon. The tendon is flaccid in comparison to the other structures and is not yet swollen. After 24 hours the tendon normally is swollen and painful. Lameness becomes more evident during this period. In both moderate and severe injury degeneration the tendon fibers can occur during the first days to 3 weeks after injury.

**Ultrasound** is the best method of making the diagnosis and quantitating the amount of tendon fiber damage. Real time or linear ultrasound scanners with a 7.5 mHz scan heads are used. A standoff is needed to reduce the artifact at the scan-head skin interface. The transverse scan provides evidence of fiber separation, fiber disruption, increased cross sectional area and peritendinous scarring. Longitudinal scans assess the fiber quality. Comparison of left and right limbs is recommended to assess increase in size, fiber density, and to discover bilateral lesions.

For your interest: Tendon lesions have been defined as type 1-4. The definition of the fiber lesion is listed below.

- **Type I lesion** - Diffuse loss of fiber density (hypoechoic).
- **Type II lesion** - Core lesion (anechoic) in 50% or less of the tendon cross sectional area.
- **Type III lesion** - Core lesion in 50% or more of the tendon cross sectional area.
- **Type VI lesion** - Core lesion which affects the entire cross section of the tendon and indicates enough fiber disruption for rupture.

Tendon lesions can progress in severity after the injury, even with rest or appropriate treatment. Tendon core lesions can increase in size. As inflammation becomes chronic, tendon cross sectional area will also increase. With re-injury the tendons become enlarged and the tendon becomes scarred with abnormal connective tissue. For these reasons, repeat ultrasound examination is important.

**Medical Treatment**

Treatment of tendinitis includes both acute therapy and rehabilitation. The initial therapy for tendinitis includes systemic and local anti-inflammatory therapy.

- **Phenylbutazone** therapy for 5-7 days is indicated.
- **DMSO** applied topically to the injured part of the tendon is used for 7-10 days.
- **Ice or cold water** is applied for 10-15 minutes three to four times daily. If ice is used the duration of time is limited so the leg won't suffer from frostbite.

This local therapy is carried on for the first 7-10 days depending on the amount of heat and swelling.
Support of the tendon with leg wraps is considered important. A bandage with adequate padding is necessary to help avoid further tendon injury from a constricting bandage and to help provide some support of the fetlock joint.

Rest is the primary treatment.

Stall rest with walking is normally required for 1-2 months. Further increases in activity are determined by the ultrasonic appearance of the tendon. The core lesion should diminish within the first 2 months followed by decrease in the cross sectional area. Turnout is often recommended, but in some cases controlled exercise including riding under saddle and swimming are helpful during the remodeling phase of tendon healing. This allows strengthening of the tendon without over use. Most race horses can start galloping after 4-5 months but the tendon should be monitored with ultrasound and scrutiny increased when sprint work is initiated. Horses should not race before 8 months after a type 2 injury and in some horses, tendons will not be ready for the stress associated with racing until after 12-14 months after the injury. A typical protocol for patient rest and tendon rehabilitation for a Type II core lesion in the middle third of the superficial digital flexor tendon is as follows.

**PROTOCOL FOR TENDINITIS: example (subject to modification depending on activity)**

- Week 1- Stall rest, no walking.
- Week 2- Stall rest, 5-10 minutes of walking twice daily.
- Week 3- Stall rest, 5-10 minutes of walking twice daily.
- Week 4- Stall rest, 10 minutes of walking twice daily.
- Week 5- Stall rest, 15 minutes of walking twice daily.
- Week 6- Stall rest, 20 minutes of walking twice daily.
*Ultrasound examination. If the core lesion is resolved start on Week 7, if the core lesion remains continue walking.
- Week 7- Walking for 30 minutes daily or turn out in a small round pen during day.
- Week 8- Walking for 30 minutes daily or turn out in a small round pen during day.
- Week 9- Walking for 30 minutes daily or turn out in a small round pen during day.
- Week 10- Walking for 30 minutes daily or turn out in a small round pen during day.
- Week 11- Riding at walk for 10 minutes.
- Week 12- Riding at walk for 10 minutes.
*Ultrasound examination. Don't start week 13 if the tendon has increased tendon areas.
- Week 13- Riding at walk for 15-20 minutes and trot for 5 minutes.
- Week 14- Riding at walk for 15-20 minutes and trot for 5 minutes.
- Week 15- Riding at walk for 30 and trot for 10 minutes.
- Week 16- Riding at walk for 30 and trot for 10 minutes.
- Week 17- Riding at walk for 30 and trot for 10 minutes.
- Week 18- Riding at walk for 30 and trot for 10 minutes.
- Week 19- Riding at walk for 45 minutes and trot for 15 minutes.
- Week 20- Riding at walk for 45 minutes and trot for 15 minutes.
*Ultrasound examination. Don’t start galloping unless the tendon area has reduced in size.
- Week 21- Light galloping.
- Week 22- Light galloping.
- Week 23 - Light galloping.
- Week 24 - Light galloping.

*Ultrasound examination. Level of training should only be increased when the tendon cross sectional area is the same or reduced and tendon fiber integrity is stable or improved.
- Weeks 25-32 - Turn out or continued training depending on monthly ultrasound results. No racing for a total of 8 months from the time of injury.

**Surgical Treatment**

Tendon splitting is used to release of the compartment pressure within an injured tendon. Tendon splitting was first used for chronic tendinitis. An increase in vascular in growth was found after tendon splitting and the chronic tendon swelling and pain was reduced. Also, Standardbreds were able to return to racing albeit at slower speeds without tendon re-injury.

Tendon splitting in the United States was tried for acute tendon injuries in the 1970's. Tendon splitting can now be completed using ultrasound guidance and tendon healing is monitored with ultrasound so horses can be rested until the healing is complete. Splitting is completed with a tendon knife or a scalpel blade. The tendon is stabbed while visualizing the entry with ultrasound. The tendon is split by rotating the blade through the tendon to in a longitudinal direction to divide the fibers rather than cut them.

Tendon splitting technique.

**Proximal check ligament desmotomy** has been used to treat acute tendinitis of the superficial flexor tendon. The rational for proximal check ligament desmotomy is release of the proximal tendon attachment to bone thereby allowing the superficial flexor muscle to stretch. Reduction in tendon tension should hypothetically release intratendinous pressure and increase elasticity at low loads.

Though there is not a good study for comparison the benefits of the proximal check ligament desmotomy versus other techniques, studies completed include increased numbers of horses holding up to racing compared to old reports. Often check ligament transection is combined with tendon splitting hoping to optimize tendon healing.
Regardless of the implementation of standard care, treatment of tendonitis can be a frustrating condition to heal. Scar tissue formation, mainly composed of collagen type III, results in poor fiber cross-linking and inferior mechanical strength. The scar tissue matrix that forms following injury has poor biomechanical properties in comparison to normal tendon and is believed to be responsible for the high incidence of re-injury. Although it has been extensively studied, equine tendonitis still lacks a highly effective treatment. Many therapeutic plans focus mainly on pain management and are accompanied by lengthy recovery times and high risk of re-injury. To overcome the relative inadequacy of traditional treatment options for equine tendonitis, veterinarians have sought to use regenerative approaches that have become extremely popular over the last decade. Regenerative therapies have included the use of autologous non-expanded material such as platelet-rich plasma, bone marrow concentrate, and adipose-derived progenitor cells (stromal vascular fraction).

Experimental studies have shown promising results in tendon healing following the use of culture expanded products such as mesenchymal stem cell (MSCs) treatment, resulting in improved tissue organization, composition and mechanics as compared to untreated control subjects. There is convincing evidence that the therapeutic benefits of MSCs are due to their well-established anti-inflammatory and immunomodulatory capability, as well as to their postulated ability to modulate local humoral and cellular tissue repair mechanisms through direct and/or paracrine signaling. Despite these encouraging reports, equine MSC therapy in tendon injury is still lacking thorough scientific awareness and specific guidelines for practical applicability. Most importantly, progress made in understanding the biology behind regenerative approaches has not corresponded to an optimization of the delivery methods as they relate to clinical outcomes in horses with tendon lesions.

Acute phase treatment

Platelet rich plasma (PRP) is an attractive alternative to traditional means of therapy in soft tissue injuries in horses because it is well established that specific growth factors contained in PRP participate in tendon and ligament repair. For example, a study using a collagenase induced superficial digital flexor tendonitis model showed that serial treatments with insulin-like growth factor I (a growth factor found in PRP) resulted in improved cell proliferation, collagen content, mechanical stiffness and sonographic appearance of treated tendons over an 8 week period. Among the growth factors abundantly present in PRP, vascular endothelial growth factor is a powerful stimulator of angiogenesis. In a model of surgically created superficial digital flexor tendon injury, the effect of PRP on neovascularization was studied using color Doppler ultrasonography and immunological staining of Factor VIII. PRP induced significantly more neovascularization than the placebo treatment until at least 23 weeks after treatment. The authors of this study speculate that a prolonged effect on neovascularization might suggest a long-lasting effect of a single intratendinous injection with PRP. Furthermore, in a similar but separate study, PRP treated tendons had a better organization of the collagen network, a higher content of glycosaminoglycans and demonstrated a higher strength at failure when compared to placebo treated tendons. Using different investigative approaches, the above studies highlight a prolonged effect of PRP treatment which may corroborate the clinical notion that, in naturally occurring tendonitis and desmitis, PRP injection does not necessitate frequent repetition. A single PRP treatment and a controlled exercise rehabilitation program were, in fact, recommended in 9 Standardbred racehorses with moderate to severe midbody suspensory...
ligament desmitis. All 9 horses returned to racing within a median time period of 32 weeks, competing at least once during the first and second years after returning to racing. Although only 5 horses raced during the third year from the injury, the authors suggest that combining intralesional PRP and a careful rehabilitation program afforded these horses an excellent prognosis for returning to racing.

Intrasyovial therapy.

Intra-synovial medications are frequently used to treat joint disease in horses. The selection of these medications depends on the joint involved, the type of joint pathology to be addressed (acute or chronic) and the expected athletic requirements of the horse. The interplay of these factors drives the selection of one or of a combination of the intrasynovial medications available. This brief overview is aimed at suggesting intrasynovial treatment options for common lameness problems arising from joint disease.

The selection of the appropriate medication is somewhat complicated by the limited choices available, although different intrasynovial products may be combined to achieve specific treatment goals. These medications are commonly used in combination and with the addition of topical, systemic parenteral or orally administered compounds aimed at treating joint pathology. In the end, the appropriate therapeutic regime should be selected on a case by case basis taking into account the expectations and possible financial constraints of horse owners and trainers.

Veterinarians should be aware of the fact that synovitis and the subsequent enzymatic degradation that occurs in the joint play a major role in the development of osteoarthritis. As a result of synovitis, enzymatic degradation of the articular cartilage will continue long after acute joint trauma has subsided even in cases in which the initial injury appeared to be mild. This is particularly true in young horses in training in which synovitis rather than joint instability is the most important factor that eventually leads to articular cartilage degeneration. The importance of early intervention in the phase of acute injury and synovitis cannot be overemphasized. In the pathogenesis of joint disease, this is the stage in which therapeutic interventions are most effective in preserving articular homeostasis for as long as possible. Extrapolating from human joint therapy, compounds have been divided into disease modifying and symptom modifying depending on whether they are administered to protect and benefit synovial membrane or cartilage or to address inflammation. As a result, it is accepted that the most effective treatments are those that combine and accomplish chondroprotection and reduce inflammation. One of the key elements of an effective treatment regime is early detection of joint disease. Unfortunately, this is not easy to accomplish because during this phase clinical signs are ill defined and standard imaging modalities are not sensitive. For this reason, veterinarians need to combine their clinical assessment with information about the horse obtained from trainers or owners. In the early stages of joint disease common complaints can be usually summarized as a general decrease in performance rather than a true lameness thus requiring keen observation skills. Relying on physical exam, joint manipulation, detection of effusion and observation of the horse in work are still...
mainstays of early detection of joint disease.

Intra-articular corticosteroids.
Methylprednisolone acetate (Depo-Medrol®), triamcinolone acetonide (Vetalog®), and betamethasone esters (Celestone Soluspan®). These are commonly used corticosteroids that injected intra-articularly serve the purpose of decreasing inflammation in the joint. In addition, Triamcinolone acetonide (Vetalog®) has been shown to have chondroprotective effects- with improved functionality of and no degradative effects on the articular cartilage. On the other hand, methylprednisolone acetate (Depo-Medrol®) had harmful effects on the cartilage at the dosages that were tested in the research setting. These in vivo studies were performed using doses ranging from 100 to 140 mg of methylprednisolone acetate have promulgated the notion that triamcinolone acetonide especially in high motion joints is the corticosteroid of choice. There have been opinions that attest that administering a lower dose would alleviate the negative effects of methylprednisolone acetate (20, 40 to 80 mg) and clinical perception may indeed support the use of this drug at these lower dosages especially for the distal tarsal joints of horses diagnosed to have osteoarthritis of these joints. Corticosteroids are commonly administered intra-articularly with hyaluronan based on a potential synergistic effect and a chondroprotective effect of this combination. The possibility of hyaluronate products diminishing the detrimental effects of methylprednisolone acetate intra-articularly has been based on anecdotal information rather than scientific evidence, but is common practice among equine practitioners and is frequently used in high and low motion joints.

Hyaluronic acid (HA) preparations.
These compounds are non-sulfated glycosaminoglycans with mild analgesic effects and more pronounced anti-inflammatory effects that result from their physical properties (steric hindrance) and pharmacological properties (inflammatory cell and mediator inhibition and mediators). Multiple studies have shown that HA inhibits inflammatory precursors such as IL-1, prostaglandin and free radicals. It has also been shown that HA secretion by synoviocytes increases in acute joint trauma and following intra-articular injection of a variety of medications including corticosteroids. This has been interpreted as a protective response by the synovium to joint inflammation providing further justification for its exogenous administration. One subject of controversy surrounds the choice of the molecular weight of the compound selected for intrasynovial therapy. Although not proven, clinical impression has driven the use of products with molecular weights greater than 1 x 106 daltons which may provide a superior chondroprotective effect and improved clinical outcomes. As an example, intra-articular hyaluronic acid combined with very low doses of corticosteroids are products of choice in the treatment of acute synovitis and capsulitis. Commonly recommended corticosteroids are triamcinolone (4 to 6 mg) or betamethasone (10 to 12 mg). Adding SURPASS® (1% diclofenac sodium IDEXX Laboratories) as a topical anti-inflammatory cream and implementing changes in the exercise routine may also be effective and often necessary treatment strategies. The use of systemic non-steroidal anti-inflammatory drugs (NSAID) for a period of time can be occasionally used as well.
**IA Adequan®.**
This polysulphated glycosaminoglycans (PSGAG) is very commonly used via the intramuscular route aimed at achieving chondroprotection. Practitioners have been historically reluctant to administer the intrasynovial preparation because of evidence of a slight increase in the risk of infection as compared to corticosteroids and HA products. Of note is that a concurrent study demonstrating that this negative effect is prevented by concurrently administering 125 mg (0.5 ml) of amikacin sulfate goes largely unnoticed. Intrasynovial PSGAG seems to be beneficial especially in horses with advanced cartilage erosion and exposure of subchondral bone.

**IRAP.**
Orthokine (or IRAP in the United States) is interleukin-1 receptor protein antagonist (IL-1ra). This product is made commercially available in the United States by Arthrex Veterinary Systems (www.arthrexvetsystems.com) The exact mechanism behind this treatment modality has not been completely clarified but it is based on the concept that stimulation of monocytes drawn from the peripheral blood would result in the upregulation of cytokines that are inherently anti-inflammatory. Although it is reasonable to believe that many molecules are up-regulated after incubation of peripheral blood, the hope is that the balance falls in favor of proteins that are “beneficial” and that the net effect results in a reduction of inflammation. One particular protein that has received attention has been IL-1ra which is hypothesized to work by binding to the interleukin-1 receptor and preventing the interaction of IL-1 with the receptor. By blocking this interaction inflammation mediated by IL-1 is reduced improving joint healing and function. Obtaining the final injectable product is straightforward but does required some moderately expensive equipment (centrifuge that accommodates 60 ml syringes and an incubator). Once obtained approximately 4 to 8ml are injected once a week for 3 treatments.

The response to treatment is variable and depends on the degree of osteoarthritis present at the time of therapy. Joints with synovitis or mild osteoarthritis seem to respond more favorably whereas subchondral bone defects or extensive cartilage damage respond less favorably. With the exception of one double blinded placebo controlled experimental study in horses in which IRAP was shown to reduce inflammation and have moderate benefit to the joint environment, there have only been anecdotal reports regarding the use of this preparation.