A Review of the Etiopathogenesis, and Current Proposed Strategies for Prevention, of Superficial Digital Flexor Tendinitis in the Horse

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Prior to skeletal maturity, energy storing tendon is exquisitely sensitive and responsive to biomechanical stimuli which promote the development of tendon tissue while after tendon growth is completed. There is very limited ability to adapt and fatigue-like accumulation of exercise-induced micro-trauma results in inevitable degeneration. Therefore, there appears to be a “window of opportunity” that may be exploited to optimize conditioning of tendon for athletic performance. Author’s addresses: Royal Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Herts, AL9 7TA, UK (Smith, Birch, Batson, Patterson-Kane, Goodman, and Cauvin) and Institute of Orthopaedics and Musculoskeletal Sciences UCL, London, UK (Goodship). © 2000 AAEP.

Introduction
Musculoskeletal injury in general, and tendon injury in particular, are major international clinical issues in the management of the equine athlete. Tendon injuries in the horse can arise by intrinsic (strain) or extrinsic (penetrations, lacerations) damage, or by displacement. The most frequently observed injury is the intrinsic or strain injury which predominantly affects the palmar soft tissue structures supporting the metacarpophalangeal joint, in particular the superficial digital flexor tendon (SDFT), but also the suspensory ligament (SL) and accessory ligament of the deep digital flexor tendon (ALDDFT).

The SDFT has a complex biological role acting not only to flex the digit and support the metacarpophalangeal joint but also to store energy for efficient locomotion. These functional roles are reflected in the gross and microscopic structure of the tendon. The pathobiology of tendon is altered by both exercise and aging. The organization of its matrix imparts elasticity for this function but it also operates close to its functional limits during maximal exercise. The SDFT is preferentially loaded during early weight bearing where strain rates in excess of 200%/second have been recorded. Any slight alteration to its structure or matrix composition can affect the mechanical properties such as stiffness.
and ultimate strength. Any change that results in an increase in stiffness will decrease energetic efficiency and may reduce athletic performance. Similarly, even subtle weakening of the structure will dramatically increase the risk of clinical tendinitis when the peak loads at maximal exercise overwhelm the structural resistance of the tendon.

The factors which promote the formation of this highly tuned system are still relatively poorly understood. However, ongoing research is providing valuable new information on the effects of age, function, and exercise. This paper reviews our current understanding of the anatomy and physiology of equine tendon and reports the results obtained from studies involving controlled exercise regimes.

Materials and Methods

These studies have involved the analysis of tendons from wild horses and working horses of different ages that had been used for different types of work under normal conditions. In addition, tendons have been analyzed from three separate controlled exercise studies:

Experiment 1—Thoroughbred fillies exercised for 18 months. Horses commenced exercise at approximately 20 months of age and were euthanized at approximately 3 years of age. Treadmill exercise was performed at the gallop 3 times a week and combined with trotting on a horsewalker 3 times a week and walking exercise for 6 days of the week. Age-matched control horses were given only walking exercise 6 days a week for 40 min per day.

Experiment 2—Thoroughbred fillies exercised for 4.5 months. Horses commenced exercise at approximately 19 months of age and were euthanized at approximately 2 years of age. Treadmill exercise was given 3 times a week and combined with trotting on a horsewalker twice a week and walking for 6 days a week. Age-matched control horses were given only walking exercise 6 days a week for 40 min per day.

Further details of these experiment exercise protocols can be found in the literature.6,7

Experiment 3—Dutch Warmblood foals. Foals were divided into three groups after 1 week with their dams: (a) box rest; (b) box rest plus training; (c) paddock exercise. The training program consisted of gallop sprints in a 48 × 15 m paddock with a sand surface on top of a concrete foundation. The number of sprints was increased from 12 at day 7 to 32 and 16 on alternate days from day 39 to weaning at 5 months. Half the foals were euthanized at this time and the remainder kept under the same conditions in a open loose box with access to a small paddock. These remaining foals were euthanized at 11 months of age.

Further details of this exercise protocol can be found in the article by van Weeren and Barneveld.8

Analysis of tendons in our laboratories has included in vitro materials testing of tendons, and light and electron microscopy for morphological studies of fibril diameter and crimp pattern. For studies into the matrix composition of tendon the dimethylmethylen blue assay was used for glycosaminoglycan levels, hydroxyproline for collagen content, cyanogen bromide cleavage for collagen type, and collagen-linked fluorescence for collagen glycosylation. COMP was quantified on tissue extracts using a competitive inhibition ELISA with an equine specfic antibody.9 Specific details of the analytical methods can be found in the references cited for each result.

Results

Biomechanical Properties and Tendon Structure

Tendon is composed of a hierarchical arrangement of linearly arranged Type I collagen fibrils which are bundled together in ever increasingly sized units to produce the fascicles seen by the naked eye on a cross-section of tendon.4 The fascicles are divided by endotenon septa, which is a looser connective tissue containing vascular and nerve elements.

The strength and mechanical properties of tendon arise from the structural organization of the matrix. Thus, the collagen fibers have a pronounced wavy, or crimp, pattern which is responsible for the non-linear behavior in the early phases of extension.4 The specific important determinants of tendon strength are not clear. The tendon will only be as strong as its weakest link, which is most likely to be in the cross-linking, covalent or electrostatic (provided by the non-collagenous proteins), between collagen fibrils or fibers.

Gross mechanical properties showed a high variance within all study groups analyzed, yet values for right and left limbs consistently showed no statistical difference.7 At specific ages, as found previously,11 there was a wide distribution of values for both stiffness and strength that do not seem to correlate with factors that normally would be expected to influence these mechanical properties. We hypothesize that individuals with low values may be predisposed to injury. The mechanical properties of the SDFT are very different to those in non-energy storing tendons such as the extensor tendons in the same individuals which are stiffer, reflecting the different function of these two tendon types.12

The collagen fibril crimp angle and length showed a regional reduction in the central core with exercise and age, with a synergistic effect.6,13–17 The differential location of this change indicates that the central fibers will straighten first under loading and therefore be more prone to rupture.

Regional differences in collagen fibril diameter were seen in long-term exercised older horses, but...
not in short-term exercised, or younger, horses. The higher proportion of small fibrils in the central region of the long-term exercised horses did not correlate with new collagen formation and thus appear to result from disassembly of the larger diameter fibril.17 Fibril diameter distributions were influenced by exercise regimens in the growing foal.

The cell population in tendons is poorly understood. Three cell types have been recognized by their nuclear morphology on light microscopy, but any difference in function between these types is unknown.4,18 Recent work has demonstrated that the cells communicate via gap junctions between long thin cytoplasmic extensions which surround the collagen fibrils and form a syncitium perfectly suited for co-ordinating cell/matrix interactions in response to mechanical loading (like bone).19

The blood supply to tendon has been considered poor in the past. However, studies using Xenon clearance have demonstrated blood flow similar to resting skeletal muscle.20 Blood flow is reduced in the areas under compression where the SDFT and DDFT wrap around the palmar aspect of the metacarpophalangeal joint but this area is usually spared of injury. Exercise and injury dramatically increases this blood flow.

Non-collagenous Matrix

On a molecular level the collagen fibrils are embedded in a non-collagenous matrix, consisting predominantly of glycoproteins. Many of these are, as yet, unrecognized but the most abundant are Cartilage Oligomeric Matrix Protein (COMP) and small proteoglycans, including decorin, fibromodulin and biglycan. COMP is a large glycoprotein which appears to be restricted in distribution to soft tissues which are loaded, such as cartilage, tendon, ligament, meniscus, and intervertebral disc. The highest levels were achieved in those tendons which receive the highest loads such as the SDF tendons, while levels are low in the extensor tendons.9 A mutation of the COMP gene in man results in pseudoachondroplasia, suggesting that this protein is important for the structural integrity of loaded tissues.21,22

The SDFT tendon matrix is relatively homogenous along its length at birth but subsequent mechanical demands result in specific matrix composition. Areas under compression induce a cartilage-like matrix consisting of type II collagen and the large proteoglycan aggrecan.23–25 The matrix component COMP increases in this region of the tendon from birth to two years of age after which levels plateau.7

The regions of the SDFT remaining under tensile loading have a matrix rich in type I collagen and small proteoglycans. These regions provide the elastic energy storage requirements and are the most common sites of injury. In the midmetacarpal tensile region of the SDFT COMP levels are also low in the neonate, increase in response to loading until they peak at 2 years of age at a much higher level than seen in the compressed areas and then decline rapidly. Removal of load from tendon at this developmental stage results in a lack of COMP accumulation in tendon, while removal of load after COMP has accumulated does not alter its levels in the tendon.7 At skeletal maturity there is a positive correlation between COMP levels in tendon and ultimate tensile strength.26

Changes in molecular composition occurred in controlled long-term exercise studies, with a reduction in GAG content and an accelerated loss of COMP in the center of the tendon.7,27 In contrast, aged horses had higher levels of type III collagen in the center of the tendon28 and subclinical injury produced an increase in both type III collagen and GAG.29 Exercise in very young foals indicated that tendons are more easily damaged during their developmental stage if the exercise level is too high.30 However, data also showed that too little exercise can also inhibit the ability of the tendon to develop. Therefore, as with other skeletal tissue development, such as cartilage, there appears to be a “window of opportunity” that may be exploited to optimize conditioning of tendon for athletic performance.

Discussion

These controlled exercise studies have also demonstrated that exercise has the effect of accelerating the ageing change and suggest that after skeletal maturity the tendon has limited ability to adapt to stress. Possible mechanisms for this progressive deterioration in the tendon matrix include vascular effects, such as hypoxia31,32 and reperfusion injury, physical effects, such as hyperthermia,33,34 and metabolic effects, such as the action of proteolytic enzymes.35 This will weaken the tendon matrix and allow the initiation of clinical tendinitis when loading overcomes the resistive strength of the tendon. Factors which increase the peak loading of the SDFT, such as weight of rider and speed of horse, will therefore also act to increase the risk of clinical tendinitis.

Further confirmation of cellular activity during growth but not after skeletal maturity has been provided by studies of gene activity in the metacarpal region of bovine tendons.36 Matrix gene expression was easily detectable in young, growing animals, but no gene activity was present in these areas in the adult. The similar responsiveness of cells recovered from both young and old tendons to growth factors and mechanical strain in vitro suggest that an absence of the appropriate growth factor stimulus may be responsible for this pattern of cellular behavior.37 Certainly, in these studies investigating TGF-β in equine tendons, there were high levels in young equine tendon, but with declining amounts after skeletal maturity.
Strategies for the Prevention of Tendinitis

Based on these results, we have advanced a hypothesis that states that prior to skeletal maturity, energy-storing tendon is exquisitely sensitive and responsive to biomechanical stimuli which promote the development of tendon tissue. After skeletal maturity there is a switch off of tendon matrix synthesis and exercise generates cumulative microdamage as the animal ages that is not repaired. This accumulation of microdamage leads to fatigue of the matrix allowing the superimposition of high loads at maximal exercise to initiate clinical tendinitis. Epidemiological studies have supported a strong association of age with the incidence of tendon injury in both horses and humans.38,39

From this hypothesis, we can suggest four strategies for the prevention of tendinitis.

Maximize the Quality of Tendon Prior to Skeletal Maturity

This could be achieved either by the early introduction of an appropriate level of exercise or improvement in any genetic determinants of tendon strength. We hypothesise that the former approach will enable us to improve the quality (strength) of the tendon matrix prior to skeletal maturity so that the subsequent inevitable decline in matrix quality will not place the tendon at risk from tendinitis until after it has completed its racing career.

Reactivate Resident Cell Populations to Repair/Remodel Fatigue Microtrauma in Older Horses

Growth factors are likely to play a major role in this process and we are currently defining those that are most important in equine digital flexor tendon. Exogenous introduction or gene therapy present options for the future in this aspect.

Prevent the Cumulative Microdamage in Adult Tendon

The mechanisms by which exercise induces cumulative damage have not been defined. One possible mechanism involves the action of proteolytic enzymes where inhibitory agents may be effective in delaying or preventing cumulative microdamage.

Improve Early Detection Using More Sensitive Ultrasonography or Serological Markers

Ultrasound technology is advancing rapidly but is still not practical for the regular monitoring of horses in training. The cumulative microdamage in tendon potentially releases matrix proteins into the blood where they may be detectable with an assay. This would provide a useful assessment of tendon health. However, this last strategy does not address the pathogenesis. We do not know whether altering training regimes we can prevent the inevitable weakening of the tendon.

Summary

Recent studies have provided considerable insight into the homeostatic mechanisms in tendons and we are now in a position to attempt to use this knowledge to reduce the incidence of tendinitis in racehorses. Because tendons repair rather than regenerate after clinical injury, prevention must be considered superior and a more realistic option to treatment. Studies are currently underway to test the first strategy for the prevention of tendinitis involving The Japan Racing Association and an international consortium of research groups (Global Equine Research Alliance [GERA] based in the United States, United Kingdom, New Zealand, and Holland).

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References

8. van Weeren PR, Barneveld A. Study design to evaluate the influence of exercise on the development of the musculoskeletal system of foals up to 11 months. Equine Vet J 1999;31:4–8.
14. Patterson-Kane JC, Firth EC, Goodship AE, et al. Age-related differences in collagen crimp patterns in the superfibi...


