Histopathology of common tendinopathies:

Update and implications for clinical management

KARIM M KHAN, JILL L COOK, FIONA BONAR, PETER HARCOURT, MATSÅSTROM

1. THE UNIVERSITY OF BRITISH COLUMBIA (SCHOOL OF HUMAN KINETICS), VANCOUVER, CANADA; THE VICTORIAN INSTITUTE OF SPORT
2. TENDON STUDY GROUP, MELBOURNE, AUSTRALIA
3. DOUGLASS HANLY MOIR PATHOLOGY, SYDNEY, AUSTRALIA
4. LUND UNIVERSITY (DEPARTMENT OF ORTHOPAEDICS), MALMO, SWEDEN

CONTENTS

SUMMARY

Tendon disorders are a major problem in competitive and recreational sports. Does the histopathology underlying these conditions explain why they often prove recalcitrant to treatment? We reviewed studies of histopathology of symptomatic Achilles, patellar, extensor carpi radialis brevis and rotator cuff tendons in sportspeople.

The literature indicates that normal tendons appear glistening white to the naked eye and microscopy reveals a hierarchical arrangement of collagen fibres in tightly-packed parallel bundles with a characteristic reflectivity under polarized light. Stainable ground substance is absent and vasculature is inconspicuous. Tenocytes are generally inconspicuous, and fibroblasts and myofibroblasts absent.

In stark contrast, tendons of symptomatic athletes appear grey and amorphous to the naked eye and microscopy reveals discontinuous and disorganised collagen fibres that lack reflectivity under polarized light. This is associated with an increase in mucoid ground substance which is confirmed with alcian blue stain. At sites of maximal mucoid change tenocytes, when present, are plump and chondroid in appearance (exaggerated fibrocartilaginous metaplasia). These changes are accompanied by increasingly conspicuous cells within the tendon tissue and most have a fibroblastic or myofibroblastic appearance (smooth muscle actin is demonstrated by using an avidin biotin technique). Maximal cellular proliferation is accompanied by prominent capillary proliferation and a tendency for discontinuity of collagen fibres in this area. Often, there is an abrupt discontinuity of both vascular and myofibroblastic proliferation just before the area of greatest abnormality. Most significant is the absence of inflammatory cells.

These findings mean that histopathologic findings in sportspeople with overuse tendinopathies are consistent with tendinosis -- a degenerative condition of unknown etiology. This finding may have implications for prognosis - i.e., the rate at which patients can return to sport after tendon symptoms.

As the common overuse tendon conditions are rarely, if at all, due to 'tendinitis' we suggest of the term 'tendinopathy' be used to describe the common overuse tendon conditions. We conclude that effective treatment of athletes with tendinopathies must target the most common underlying histopathology, tendinosis, a non-inflammatory condition.

INTRODUCTION

The specific pathology underlying a patient's symptoms determines prognosis and influences choice of treatment. For example, retrosternal chest pain of cardiac origin has a different natural history and treatment to apparently identical pain referred from the thoracic spine. Similarly, prognosis and treatment of a benign breast fibroadenoma differs radically from an apparently identical lump that is carcinoma. Do such varying pathologies also underlie the painful tendon conditions that cause a great deal of morbidity [1]?

In this review of the histopathology of the common overuse tendon conditions, we use the term 'tendinopathy' [2-4] as a generic descriptor to include all pathologies that arise in and around tendons. Thus, tendinitis, tendinosis and paratenonitis (all defined below) are specific examples of tendinopathy, just as greenstick fracture, stress fracture and compound fracture are specific examples of the generic category 'fracture'.

After providing a background description of normal tendon anatomy, the aims of this review are fourfold:

- to review the histopathology underlying Achilles, patellar, extensor carpi radialis brevis and rotator cuff tendinopathies.
- to discuss whether a single histopathology appears common to a majority of tendinopathies.
- to examine whether current management has a rational basis given the histopathology most commonly present.
- to suggest directions for further research.

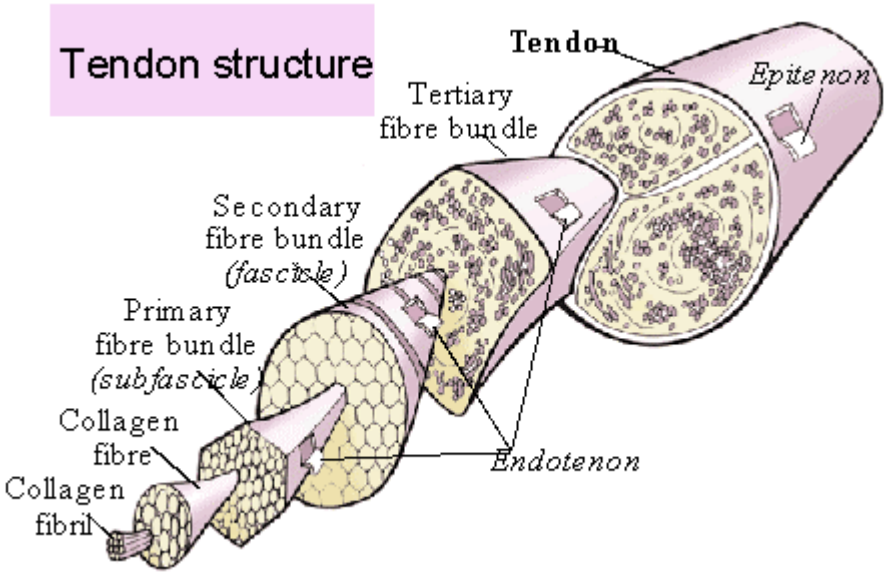
1. NORMAL TENDON ANATOMY

In this section we summarise the macroscopic and light microscopic appearance of normal tendon so the reader can better understand the abnormalities found in symptomatic tendons. More detailed descriptions of tendon anatomy exist elsewhere [2, 5, 6].

1.1 Tendon constituents

Tendons are anatomic structures interposed between muscles and bones that transmit the force created in muscle to bone and make joint movement possible [5]. The basic elements of tendon are collagen bundles, cells, and ground substance or extracellular matrix, a viscous substance rich in proteoglycans. Collagen provides tendon with tensile strength, ground substance provides structural support for the collagen fibres and regulates the extracellular assembly of procollagen into mature collagen [7]. Tenocytes, flat tapered cells sparingly distributed among the collagen fibrils [7], synthesize both the ground substance and the procollagen building blocks of protein. Collagen is arranged in hierarchical levels of increasing complexity beginning with tropocollagen, a triple-helix polypeptide chain, which unites into fibrils, fibres (primary bundles), fascicles (secondary bundles), tertiary bundles and finally the tendon itself [5, 7] (Figure 1).

Fig. 1. The hierarchical organization of tendon structure: from collagen fibrils to the entire tendon (reproduced from Jozsa & Kannus, [5] with permission).



The entire tendon is covered by the epitenon, a fine, loose connective tissue sheath containing the vascular, lymphatic and nerve supply. The epitenon extends deeper into the tendon between the tertiary bundles as the endotenon. More superficially, the epitenon is surrounded by paratenon, a loose areolar connective tissue consisting essentially of type I and type III collagen fibrils [8] some elastic fibrils and an inner lining of synovial cells [9]. Together, the paratenon and epitenon are sometimes called the peritendon [5]. The classic two-layered synovial tendon sheath is only present in certain tendons as they pass areas of increased mechanical stress. The outer layer is the fibrotic (ligamentous) sheath and the inner layer is the synovial sheath which consists of thin visceral and parietal sheets [5]. The myotendinous junction is a highly specialized anatomic region in the muscle-tendon unit where tension generated by muscle fibres is transmitted from intracellular contractile proteins to extracellular connective tissue proteins (collagen fibrils) [5]. As this region is rarely affected by tendinopathy its complex ultrastructure is not discussed further but the interested reader is referred elsewhere [5]. The osteotendinous junction is a specialized region in the muscle-tendon unit where the tendon inserts into a bone. In the osteotendinous junction, the viscoelastic tendon transmits the force into a rigid bone. The region has been described as containing four light-microscopic zones: (1) tendon, (2) fibrocartilage, (3) mineralized fibrocartilage and (4) bone [10, 11].

1.2 Light microscopic appearance of collagen

The light microscopic appearance of normal tendon warrants further description as this is the key outcome measure in studies of histopathology of overuse tendinopathies. Normal tendon consists of dense, clearly defined parallel and slightly wavy collagen bundles. Collagen has a characteristic reflective appearance under polarised light. Between the collagen bundles there is a fairly even sparse distribution of cells with thin wavy nuclei. There is an absence of stainable ground substance and no evidence of fibroblastic or myofibroblastic proliferation. Tendon is supplied by a network of small arteries oriented parallel to the collagen fibres in the endotenon [5, 12, 13].

2. HISTOPATHOLOGY UNDERLYING COMMON TENDON OVERUSE CONDITIONS

2.1 Achilles tendon

Studies of the histopathology of symptomatic Achilles tendons reveal (i) degeneration and disordered arrangement of collagen fibres and (ii) an increase in vascularity. Collagen degeneration was reported in numerous studies [14-22]. Although at least six different subcategories of collagen degeneration have been described [5], Achilles tendon degeneration is usually either - 'mucoid' or 'lipoid' [5].

Mucoid degeneration causes the affected region to soften, lose its normal glistening white appearance and become grey or brown. Light microscopy reveals collagen fibres that are thinner than normal. Large mucoid patches and vacuoles are present between fibres. There is an increase in Alcian-blue-staining ground substance. Lipoid degeneration, as the name implies, refers to an abnormal accumulation of lipid in tendon tissue [5]. In addition to collagen fibres in symptomatic Achilles tendons being abnormal in themselves, the characteristic hierarchical structure is also lost [16, 19, 21, 23, 24].

In symptomatic Achilles tendons vascularity was increased and blood vessels randomly oriented, sometimes at right angles to collagen fibres [9, 17, 19, 20, 24, 25]. Inflammatory lesions [14, 15, 18, 25] and granulation tissue [9, 14, 17, 18] were infrequent, and when found, were in association with partial ruptures.

In a landmark study, Astrom and Rausing undertook histopathologic examination of 163 patients (75% of whom participated in nonprofessional sports, particularly running) who had had classical symptoms and signs of Achilles tendinopathy for a median of 18 months (range 3 months-30 years) [12]. The authors reported an obvious change in collagen fibre structure with loss of the normal parallel bundles. Collagen appeared more diffuse and bundles coalesced. Birefringence to polarised light was reduced or lost. There was an increase in mucoid ground substance. There was an increase in the number of cells with rounded nuclei, even in cases where symptoms had only been present for a relatively short time. Neovascularisation was noted. Signs of bleeding, that is, erythrocytes and positive staining for iron pigment, were occasionally present.

In partial ruptures, frayed tissue was bordered by fibrin deposits but histopathology remained identical to those cases without rupture. 'Inflammatory cells, intracellular lipid aggregates and acellular necrotic areas were exceptional' and not regarded as normal elements of the degenerative process [12]. The authors concluded that 'the absence of inflammation and the poor healing response demonstrate a state of degeneration that conforms to the histopathology described by previous authors in total ruptures and in chronic tendinopathy' [12].

With respect to the paratenon, Kvist et al. [8, 26, 27] found evidence of mucoid degeneration, fibrosis and vascular proliferation with a slight inflammatory infiltrate only - similar to other series [9, 16, 20, 21, 25, 28]. Astrom and Rausing [12] found virtually no evidence of paratenonitis in their series of Achilles tendon specimens. These differences may be explained by the fact that Kvist et al. did not report pathology of the tendon itself, and studied more active, younger patients [8, 26, 27]. Thus, paratenonitis is not a prerequisite for Achilles tendon symptoms in a population of recreational sportspeople and office workers. The major lesion in chronic Achilles tendinopathy 'is a degenerative process characterized by a curious absence of inflammatory cells and a poor healing response' [12].

Achilles tendon degeneration is evident as increased signal on MR imaging [29] and hypoechoic regions on ultrasound [30-32]. These areas of abnormal imaging correspond with areas of altered collagen fibre structure and increased inter-fibrillar ground substance, which proved to consist of hydrophilic glycosaminoglycans [29, 33, 34] .

2.2 Patellar tendon

As recently as 1994 it was reported that the pathology underlying patellar tendinopathy was not clearly defined [35]. This reflects confusion arising from differences in nomenclature, rather than a paucity of data [3, 4, 13, 36]. Macroscopically, the patellar tendon of patients with patellar tendinopathy (also commonly called jumper's knee) contain soft [37], yellow-brown and disorganised tissue in the deep posterior portion of the patellar tendon adjacent to the lower pole of the patella [37-39] evident even to the naked eye [40-45]. This macroscopic appearance is commonly labelled as 'mucoid' degeneration [40, 43-47]. Occasionally, authors have reported 'hyaline' degeneration [39, 41], which is characterised by hardness of the tendon rather than the softness seen in mucoid degeneration [5]. Histologically, however, alcian blue stain highlights 'hyaline' change [41] confirming that this change represents advanced mucoid degeneration (see below).

Under the light microscope, the tendons of patients suffering jumper's knee do not consist of tight parallel collagen bundles but instead are separated by increased mucoid ground substance that gives them a disorganised and discontinuous appearance. Clefts in collagen and occasional necrotic fibres may suggest microtearing [44, 48]. There is loss of the characteristic reflective polarised light appearance [13].

A consistent feature across studies of the patients with chronic patellar tendinopathy was the finding of mucoid degeneration with variable fibrosis and neovascularisation. The collagen producing tenocytes themselves lost their fine spindle shape and nuclei were more rounded and sometimes chondroid in appearance amounting to fibrocartilaginous metaplasia [40, 44, 49]. Small vessel ingrowth was also evident [40, 44-46]. As with Achilles tendinopathy, patellar tendinopathy occasionally revealed erythrocytes and positive staining for iron pigment but the histopathology remained identical to those cases without rupture [13].

Virtually every study of the histopathology of patellar tendinopathy reported that cells were more conspicuous and more common than in normal tendon. This increased cellularity is due to fibroblasts [40, 43-46, 50-52] and board-certified pathologist authors have found inflammatory cells to be absent [13, 41]. None of the papers that reported the presence of inflammatory cells reported staining methods or the expertise of pathologist that reviewed the specimens [39, 42, 53-55] and only one [53] included a pathologist author.

Regions of tendon degeneration produce increased signal on MR imaging [13, 41] and hypoechoic regions on ultrasound [13, 52, 56]. This phenomenon appears to correspond to mucoid degeneration [13]. These regions can be found in asymptomatic jumping athletes [57, 58] and do not necessarily predict symptoms [59]. Thus, it appears that tendinosis commonly underlies patellar tendinopathy, but that subclinical levels of tendinosis may also occur [60, 61].

2.3 Extensor carpi radialis brevis tendon

The term 'tennis elbow' was introduced in the 1880s but it was not until 1979 that pathology of the extensor carpi radialis brevis tendon was associated with lateral tennis elbow [62]. At surgery in over 600 cases of lateral tennis elbow, Nirschl found the extensor carpi radialis brevis tendon to contain disrupted collagen fibres, increased cellularity and neovascularisation [63]. Acute inflammatory cells were almost always absent from the tendon, but a mild sprinkling of chronic inflammatory cells were noted in supportive, or adjacent tissues. When chronic inflammatory cells were present, they resulted from repair of partial tears [63]. Although Nirschl coined the term 'angiofibroblastic hyperplasia' for the histology seen in elbow tendinosis [62], presumably to emphasize the neovascularisation (angio) and increased cellularity (fibroblastic), these features are both typical of the well-recognised pathological entity of tendinosis (see below).

A recent study in 20 cases of chronic (6-48 months) lateral 'epicondylitis' confirmed that areas of abnormal tissue on imaging corresponded with areas of neovascularization, disruption of collagen and mucoid degeneration on histopathologic examination [64]. There was no histopathologic evidence of either acute or chronic inflammation in any of the specimens [64].

Similarly, the histopathology reported in lateral tennis elbow also exists in medial tennis elbow [63, 65]. There was no macroscopic evidence of either acute inflammation or acute inflammatory cells. There was loss of the normal parallel bundle appearance of collagen, an increase in tenocyte numbers and neovascular infiltration [63, 65].

2.4 Rotator cuff

Histopathology of symptomatic rotator cuff tendons reveals mucoid degeneration and fibrocartilaginous metaplasia [66] as well as cellular distortion and necrosis, calcium deposition, fibrinoid thickening, hyalinization, fibrillation and microtears. There is loss of the characteristic crimped pattern of tendon and parallel bundles of collagen separate and become disorganised [66-69].

As early as the 1930s and 40s Codman described rotator cuff 'rim rent' which was localised disruption of the innermost fibres of the supraspinatus tendon attaching most closely to the articular surface of the humeral head [70] and Wilson reported degenerative processes to be the basis of rotator cuff tendinopathy [71]. Also in the 1940s, McLaughlin showed insertional tendinopathy of the external rotators of the shoulder consisted of calcification, hyaline degeneration (characterised by the hypocellularity, vacuolation, nuclear pyknosis, more homogeneous matrix and decreased eosinophilia -- all of which probably represent mucoid degeneration) and

microtears without inflammation in the tendon tissue [72]. Sometimes fibrocartilaginous metaplasia was found [72].

Cadavers of individuals who had had symptomatic rotator cuff tendinopathy also revealed degenerative changes with an absence of inflammation [11]. Uhthoff and Sano found 'disruption of fascicles, formation of foci of granulation tissue, dystrophic calcification, thinning of fascicles, associated with cell and vessel proliferation' [73]. They demonstrated a correlation between the degree of degenerative changes described and the load at tendon failure. It is noteworthy that when these authors examined bursal tissue in patients with so-called subacromial 'bursitis' they found an 'absence of plasma cells and a paucity or even absence of neutrophils and lymphocytes'. These features are incompatible with true inflammatory bursitis as seen in, for example, rheumatoid arthritis.

The commonly accepted belief that tendon degeneration results from hypovascularity may not be based on sound evidence. Hypervascularity of the degenerative rotator cuff has been reported [74, 75]. Regions of tendon degeneration produce high intensity signal on MR imaging [69]. A high proportion of asymptomatic volunteers (89-100%) have regions of high signal in the rotator cuff tendon [76-79]. This suggests, but does not prove, that subclinical tendon degeneration may be a relatively common phenomenon amongst asymptomatic individuals.

3. HISTOPATHOLOGY OF OVERUSE TENDON CONDITIONS IS GENERALLY TENDINOSIS

Lack of consistent nomenclature for histopathologic findings has limited progress in understanding the pathological basis of tendinopathy. Various classifications have been proposed [5, 49, 80] but have their limitations [5]. Bonar's modification of Clancy's classification is tabled (Table 1).

Table 1. Bonar's modification of Clancy's classification of tendinopathies [49]

Pathological diagnosis	Concept (macroscopic pathology)	Histologic finding
Tendinosis	Intratendinous degeneration (commonly due to ageing, microtrauma, vascular compromise)	Collagen disorientation, disorganisation and fibre separation by an increase in mucoid ground substance, increased prominence of cells and vascular spaces with or without neovascularization and focal necrosis or calcification
Tendinitis/ Partial rupture	Symptomatic degeneration of the tendon with vascular disruption and inflammatory repair response	Degenerative changes as noted above with superimposed evidence of tear, including fibroblastic and myofibroblastic proliferation, haemorrhage and organising granulation tissue.
Paratenonitis	'Inflammation' of the outer layer of the tendon (paratenon) alone, whether or not the paratenon is lined by synovium	Mucoid degeneration in the areolar tissue is seen. A scattered mild mononuclear infiltrate with or without focal fibrin deposition and fibrinous exudate
Paratenonitis with tendinosis	Paratenonitis associated with intratendinous degeneration	Degenerative changes as noted in tendinosis with mucoid degeneration with or without fibrosis and scattered inflammatory cells in the paratenon alveolar tissue

3.1 Tendinosis

Although the term tendinosis was first used by German workers in the 1940s, its recent usage results from the work of Puddu et al. [21]. Tendinosis is tendon degeneration without clinical or histological signs of an inflammatory response. Tendinosis can be associated with paratenonitis (e.g., in the Achilles tendon [25]). Collagen degeneration with fibre disorientation, increased mucoid ground substance, and an absence of

inflammatory cells was the characteristic pathology of the tendinopathies described in the previous section. Thus, it appears that tendinosis is the major, and perhaps the only clinically relevant chronic tendon lesion although minor histopathologic variations may exist in different anatomical sites. Paratenonitis is described in the Achilles tendon but is generally poorly documented and tendinitis appears rare, if it exists at all.

The light microscopic findings of tendinosis occur in collagen, among tenocytes and also within the matrix or ground substance [81]. Some collagen fibres appear to separate giving the impression of loss of their parallel orientation, there is a decrease in fibre diameter, and a decrease in overall density of collagen. Collagen microtears also occur and these may be surrounded by erythrocytes, fibrin and fibronectin deposits. Within collagen fibres there is unequal and irregular crimping, loosening and increased waviness, in contrast to the normal tight parallel bundled appearance. There is an increase in Type III (reparative) collagen. These changes lead to decreased birefringence of the tendon under polarised light microscopy [81]. Special stains consistently demonstrate and increase in mucoid ground substance (proteoglycans) [33, 34].

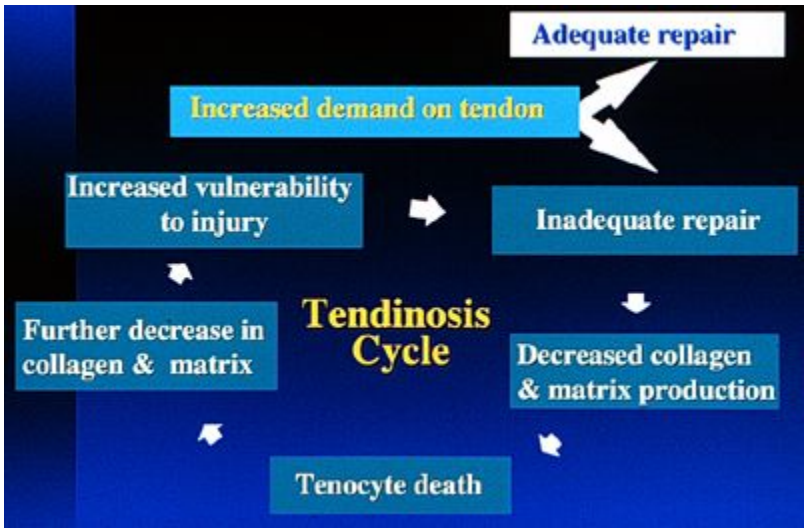
There is great variation in cellular density in tendinosis. In some areas tenocytes are abnormally plentiful and have rounded nuclei and ultrastructural evidence of increased production of proteoglycan and protein which gives them a chondroid appearance. In contrast, other areas of the tendon may contain fewer tenocytes than normal and those remaining have small, pyknotic nuclei [81]. Rarely, there is infiltration of lymphocytes [81] and macrophage type cells, which may be part of a healing process. A characteristic feature of tendinosis is proliferation of capillaries and arterioles.

Various morphologic expressions of tendinosis have been described:

- hypoxic degeneration,
- hyaline degeneration,
- mucoid or myxoid degeneration,
- fibrinoid degeneration,
- lipoid degeneration,
- calcification,
- fibrocartilaginous and bony metaplasia [2, 5].

These pathologies can coexist and their prevalence varies, possibly depending on the anatomical site and the nature of the insult that caused them (e.g. hypoxia versus mechanical loading, acute versus chronic injury). Thus, tendinosis is the end result of a number of etiologic processes with fairly small spectrum of histological manifestations. The essence of tendinosis is degeneration in tendon cells, collagen fibres and the subsequent increase in noncollagenous matrix [5] (Table 2). Leadbetter has proposed a theoretical model to illustrate how tendon injury may precipitate tendinosis (Figure 2).

Figure 2. A theoretical model of the tendinosis cycle (modified from Leadbetter [80]).



The finding that the clinical tendon conditions in sportspeople are due to tendinosis is not new. Writing about the tendinopathies in 1986, Perugia et al. noted the "remarkable discrepancy between the terminology generally adopted for these conditions (which are obviously inflammatory since the ending 'itis' is used) and their histopathologic substratum, which is largely degenerative" [2].

3.2 Tendinitis

Tendinitis is a condition in which the substance of tendon exhibits an inflammatory response. Many knowledgeable tendon physicians and scientists understand that when the term 'tendinitis' is used in a clinical context it refers to a clinical syndrome and not a specific histopathologic entity [35, 73]. It could be argued that this 'accepted' misuse of the term does not warrant alteration. However, while the term 'tendinitis' remains in use for what is truly tendinosis, some clinicians, as well as athletes, coaches and patients, will underestimate the significance of the condition. Hence an increasing number of workers recommend that the misnomer tendinitis should be abandoned [12, 13, 21, 63, 69, 80, 82-84].

Although there has been no convincing evidence of the histopathology that would correspond to true 'tendinitis' in humans, it must be acknowledged that in studies where rabbit Achilles tendons were divided and then repaired, inflammatory cells including neutrophils were present at postoperative day 5 and then disappeared by day 18 [85]. Clearly this model does not replicate overuse tendinopathy, but until appropriate biopsies are obtained in humans the possibility of a brief period of true 'tendinitis' cannot be totally excluded. In clinical practice, most tendinopathies are chronic (i.e., tendinosis) when the patient seeks medical attention.

3.3 Paratenonitis

Paratenonitis occurs where a tendon rubs over a bony protruberance. The term has been proposed as an umbrella term for the separate entities of peritendinitis, tenosynovitis (single layer of areolar tissue covering the tendon) and tenovaginitis (double-layer tendon sheath). Examples include paratenonitis of the abductor pollicis longus and extensor pollicis longus (De Quervain's disease), and of the flexor hallucis longus as it passes the medial malleolus of the tibia [5, 86].

Paratenonitis is characterised clinically by acute oedema and hyperaemia of the paratenon with infiltration of inflammatory cells (Table 1). After hours to a few days, fibrinous exudate fills the tendon sheath and causes the 'crepitus' that can be felt on clinical examination. In chronic paratenonitis, fibroblasts appear along with a perivascular lymphocytic infiltrate. Peritendinous tissue becomes macroscopically thickened and new connective tissue adhesions occur [81]. Myofibroblasts, cells with cytoplasmic myofilaments also appear and make up about 20% of the noninflammatory cells. These cells are capable of active contraction, indicating that scarring and shrinkage associated with paratenonitis is an active, cell-mediated process [81]. Blood vessels proliferate. Marked inflammatory changes are seen in more than 20% of the arteries [87]. Thus, inflammatory cells are found in both the cellular elements of the tendon and the vascular ingrowth. Despite these data, the experience of certain pathologists (including FB) and scientists (including MS) in this field, is that inflammation is rare.

ARE CURRENT TREATMENTS APPROPRIATE FOR TENDINOSIS?

Treatment of any organic medical condition is ideally based on understanding of pathophysiology. For example, insulin-dependent diabetes, a condition of inadequate insulin production, is treated by providing exogenous insulin. Unfortunately, chronic overuse tendon conditions in athletes have been treated as inflammatory conditions [88] when their histopathology clearly reveals degenerative tendinosis. Furthermore, very few rigorous studies [89], have tested the efficacy of the empirically-based treatment protocols [90,91]. In this section we review the common methods used to treat tendinopathies in clinical practice and speculate as to their potential mechanism of action in tendinosis.

4.1 Relative rest

Tendinosis, structural damage to the tendon that may include partial tearing of collagen, may require longer healing time than has traditionally been afforded a patient with tendinopathy. In sports, tendons must often sustain more than 10 times body weight, yet the tissue has a slow metabolic rate as evidenced by its having only 13% of the oxygen uptake of muscle and requiring more than 100 days to synthesize collagen [94, 95]. Thus, repair of tendinosis may take months rather than weeks.

Leadbetter [80] has postulated that tissue damage is already advanced when an athlete first notices tendon pain (Figure 3). If this is the case , then it would suggest that even patients who present with only a few days of symptoms may require relative rest to permit tendon damage to repair. Estimates of the rate of tenocyte repair vary, but some studies suggest that two to three weeks are required for a tissue response to occur [5]. After that time, gradual tendon strengthening may be indicated.

Figure 3. Schematic illustration of pain and tissue damage in overuse tendinopathy. Tendon pathology may begin well before symptoms arise. Therefore, recovery may take months, even in patients who present with recent onset of symptoms. Adapted from Leadbetter [80].

4.2 Strengthening

Strengthening, particularly eccentric strengthening, has been advocated as a treatment of tendon overuse conditions since the early 1980s [93, 96, 97]. Clinical studies point to the efficacy of eccentric strengthening regimens [89, 93, 96-98]. Mechanical loading accelerates tenocytes metabolism and may speed repair [99]. Using a rabbit Achilles tendon model, Enwemeka and colleagues [100] found that the combination of laser and early mechanical loading of tendons increased collagen production. These data provide rationale for judicious, progressive strengthening in the treatment of tendinosis [101].

4.3 Nonsteroidal anti-inflammatory drugs (NSAIDs)

On theoretical grounds one would predict that the anti-inflammatory action of NSAIDs would have no therapeutic effect in tendinosis, a non-inflammatory condition. Furthermore, the analgesic effect of NSAIDs [102] may permit patients to ignore early symptoms, further damage tendon and thus, delay definitive healing. In practice, the clinical role of NSAIDs in tendinosis has not been evaluated systematically [103] although Astrom et al. found no beneficial effect of NSAIDs in patients with Achilles tendinopathy [104]. However, the possibility remains that NSAIDs could benefit patients with tendinosis via alternate mechanisms such as accelerated formation of cross-linkages [102, 105, 106].

4.4 Corticosteroids

The role of corticosteroids in treatment of tendon conditions has been the subject of considerable debate [107, 108] but very few well-designed studies [108]. Further studies are desperately needed. It is clear that corticosteroid injection into tendon tissue leads to cell death and tendon atrophy [63]. As tendinosis is not an inflammatory condition, the rationale for using corticosteroids needs reassessment, particularly as corticosteroids inhibit collagen synthesis [109, 110] and decrease load to failure [111].

4.5 Other pharmaceutical agents

The protease inhibitor aprotinin and other drugs such as low dose heparin have been used in the management of peri- and intratendinous pathology [112-114]. Glycosaminoglycan polysulphate, one of the constituents of ground substance, has also been advocated for treatment of tendinopathy [115, 116].

4.6 Modalities

Physiotherapists employ a wide variety of modalities including ultrasound, laser, and heat to treat tendinopathies [88, 117]. Modalities are proposed to decrease inflammation and promote healing but 'there is only limited evidence as yet to support many of these claims' [88]. Studies of severed tendons have shown that ultrasound increases collagen synthesis in fibroblasts [118] and increases tensile strength of healing tendon [119, 120] and has little effect on inflammation [121, 122]. After rabbit Achilles' tenotomy there was a 26% greater collagen concentration in tendons that had received laser photostimulation compared with those that received sham laser [123]. Biomechanical and biochemical measures of tendon healing were improved by a combination of ultrasound, laser and electrical stimulation of rabbit Achilles tendons after tenotomy and suture repair [124]. All of these effects would help to reverse the pathology of tendinosis by stimulating fibrosis and repair.

4.7 Cryotherapy

Cryotherapy may decrease the extravasation of blood and protein from the new capillaries found in tendinosis [117]. It would also be expected to decrease the metabolic rate of tissue. Thus, ice may play a role in treating tendinosis. Ice would be particularly effective in treating tendinopathies where paratenonitis is associated with tendinosis (e.g., some Achilles tendinopathies). As ice may mask pain in tendinosis, it ought not be used prior to sports participation.

4.8 Braces and supports

Braces and supports are used as an adjunct to treatment of elbow and knee tendinopathies. Braces may act to keep the tendon warm during sporting performance but would not be expected to protect the tendon except by aiding proprioception. Rigid strapping support, such as has been advocated in the treatment of tennis elbow [92],

may serve to decrease the load on the extensor carpi radialis brevis tendon by reinforcing the tendon origin.

4.9 Orthotics

Orthotics are commonly prescribed in the treatment of Achilles tendinopathy and less commonly, for jumper's knee [92]. Assuming that the symptomatic athlete has a biomechanical abnormality, it would appear plausible that the orthotic would reduce the load through the tendon, and thus serve as a positive factor toward tendon healing. However, strongly opposing views exist [125] and further studies of biomechanics in athletes with tendinopathies are required.

4.10 Technique correction

As technique correction aims to decrease the load that is placed through a tendon, it clearly has a place in managing the tendinosis associated with overuse conditions [126]. For example, attention to a tennis player's backhand drive technique can play a major role in treating tendinosis at the lateral elbow [63] and adjusting jumping technique in volleyballers may contribute to treatment of patellar tendinosis [127].

4.11 Surgery

The aims of surgery have been outlined elsewhere [128] and clinical research suggests it can be effective [129, 130]. Why surgery promotes healing of tendon is still not understood [91]. It has been argued that perhaps the postoperative healing response and the careful progression of rehabilitation after surgery, rather than the surgery itself, causes improvement in the patient's condition [88, 91].

5. FUTURE DIRECTIONS

The preceding section indicates that many questions fundamental to rational treatment of tendinopathies remain unanswered [3, 131]. To attract research funding from major governmental granting agencies to address these questions, sports medicine researchers may need to increase their focus on occupation-associated tendinopathies as well as continuing their interest in sports-related tendinopathies.

Basic science research is needed to better understand the control of collagen synthesis [132]. The natural history of tendon healing warrants study [133, 134] as does the role of mechanical loading in stimulating or delaying the repair process [135]. The efficacy of the numerous physical modalities in influencing tendon healing requires investigation. Studies of tendon biochemistry may reveal a number of key matrix components and permit pharmacological manipulation of tendon ground substance to accelerate healing. Animal models have been used to study the biomechanical strength of isolated in-vivo tendon tissue [136] before and after training programs [137] and such studies may provide a pathway to understanding how strengthening affects tenocytes.

Clinical research is needed in both conservative and surgical aspects of management of tendinosis [3, 91, 130]. Empirically determined conservative protocols need to be tested and this is likely to need multi-centre cooperation to achieve adequate statistical power. Clinical tendon research would benefit greatly from having specific rating scales for assessing severity of symptoms and degree of disability in various tendinopathies. The VISA scale [36, 138] provides such a reproducible tool for patellar tendinopathy, but objective outcome measures are needed for other tendinopathies also.

Simple clinical questions that have not been answered include: 'How long should a tendon be rested when a patient first presents with symptoms of tendinopathy?'; 'What is the role of physical modalities including ice in treating tendinopathies?'; 'Does therapeutic massage accelerate tendon healing?'; 'Do NSAIDs or corticosteroids accelerate tendon healing?'; 'What is the best protocol for strengthening of a tendon with tendinosis?'; 'What are the indications for tendon surgery?'

Research into the surgical management of tendinosis should aim to provide evidence for the best type of operation for each tendon and the optimal rehabilitation protocol (including immobilisation after surgery, if any). Examination of various papers reporting surgical treatment of tendinopathies reveals a wide range of surgical practices [130, 139] - a fairly convincing sign that none is ideal.

Further study of imaging modalities in tendinosis are needed [57, 59, 140,141]. If a form of imaging (such as specific MR sequences) were able to predict that symptoms were imminent in high-risk athletes this would be a boon for clinicians and patients. There is also a need for imaging criteria that can assist in determining when conservative management has failed. At present there are no effective guidelines to determine whether a patient with chronic tendon symptoms requires further conservative management or whether surgery is indicated. The

significance of postoperative tendon imaging abnormalities remains unclear [142].

6. CONCLUSION

Tendon conditions cause a great deal of morbidity in both elite and recreational athletes and outcome of treatment is often unsatisfactory. Evidence that the common clinical conditions (e.g. Achilles, patellar, elbow and rotator cuff tendinopathies) are due to tendinosis has been present for many years, yet the misnomer 'tendinitis' is still widely used for these conditions in clinical practice. Treatment may not fully address the problem of tendinosis. This review supports the increasingly-widely held position that the majority of sports related tendinopathies are due to tendinosis. Clinical management and further research should reflect this fundamental precept.

REFERENCES

1. Kannus P: Tendons-a source of major concern in competitive and recreational athletes. [Editorial]. Scand J Med Sci Sports 7:53-54, 1997.

2. Perugia L, Postacchini F, Ippolito E. The tendons. Biology, pathology, clinical aspects.Milano: Editrice Kurtis s.r.l., 1986.

3. Khan KM, Maffulli N: Tendinopathy: an Achilles' heel for athletes and clinicians. [Lead editorial]. Clin J Sports Med 8:151-154, 1998.

4. Maffulli N, Khan KM, Puddu G: Overuse tendon conditions. Time to change a confusing terminology. Arthroscopy 14:840-843, 1998.

5. Józsa L, Kannus P. Human tendons. Champaign, Illinois: Human Kinetics, 1997:576.

6. O'Brien M: Structure and metabolism of tendons. Scand J Med Sci Sports 7:55-61, 1997.

7. Astrom M. On the nature and etiology of chronic achilles tendinopathy [PhD]. Lund University, Sweden, 1997.

8. Kvist M, Jozsa L, Jarvinen M, et al.: Fine structural alterations in chronic Achilles paratenonitis in athletes. Path Res Pract 180:416-423, 1985.

9. Williams JG: Achilles tendon lesions in sport. Sports Med 3:114-135, 1986.

10. Cooper RR, Misol S: Tendon and ligament insertion: A light and electron microscopic study. J Bone Jt Surg 52-A:1-20, 1970.

11. Becker W, Krahl H. Die Tendinopathien (Grundlagen, Klinic, Therapic). Stuttgart: G Thieme Verlag, 1978:9-19.

12. Astrom M, Rausing A: Chronic Achilles tendinopathy. A survey of surgical and histopathologic findings. Clin Orthop 316:151-164, 1995.

13. Khan KM, Bonar F, Desmond PM, et al.: Patellar tendinosis (jumper's knee): findings at histopathologic examination, US and MR imaging. Radiology 200:821-827, 1996.

14. Denstad TF, Roaas A: Surgical treatment of partial Achilles tendon rupture. Am J Sports Med 7:15-17, 1979.

15. Fox JM, Blazina ME, Jobe FW, et al.: Degeneration and rupture of the Achilles tendon. Clin Orthop 107:221-224, 1975.

16. Harms J, Biehl G, von Hobach G: Pathologie der Paratenonitis achillea bei Hochleistungssportlern. Arch Orthop Unfallchir 88:65-74, 1977.

17. Kalebo P, Goksor L-A, Sward L, et al.: Soft tissue radiography, computed tomography and ultrasonography of partial Achilles tendon ruptures. Acta Radiol 31:565-70, 1990.

18. Ljungqvist R: Subcutaneous partial rupture of the Achilles tendon. Acta Orthop Scand Suppl 113 (suppl):1-86, 1967.

19. Merkel KH, Hess H, Kunz M: Insertion tendinopathy in athletes. A light microscopic, histochemical and electron microscopic examination. Pathol Res Pract 173:303-309, 1982.

20. Nelen G, Martens M, Burssens A: Surgical treatment of chronic Achilles tendinitis. Am J Sports Med 17:754-759, 1989.

21. Puddu G, Ippolito E, Postacchini F: A classification of Achilles tendon disease. Am J Sports Med 4:145-150, 1976.

22. Benazzo F, Stennardo G, Valli M: Achilles and patellar tendinopathies in athletes: pathogenesis and surgical treatment. Bull Hosp Jt Dis 54:236-240, 1996.

23. Burry HC, Pool CJ: Central degeneration of the achilles tendon. Rheumatol Rehabil 12:177-181, 1973.

24. Burry HC: The pathology of the painful heel. Br J Sports Med 6:9-12, 1971.

25. Clancy WGJ, Neidhart D, Brand RL: Achilles tendonitis in runners: A report of 5 cases. Am J Sports Med 4:46-57, 1976.

26. Kvist M, Jozsa L, Jarvinen M, et al.: Chronic Achilles paratenonitis in athletes: A histological and histochemical study. Pathology 19:1-11, 1987.

27. Kvist M, M Lehto, Jozsa L, et al.: Chronic Achilles paratenonitis. An immunohistologic study of fibronectin and fibrinogen. Am J Sports Med 16:616-623, 1988.

28. Snook GA: Achilles tendon tenosynovitis in long-distance runners. Med Sci Sports Exerc 4:155-158, 1972.

29. Movin T, Kristoffersen-Wiberg M, Rolf C, et al.: MR imaging in chronic Achilles tendon disorder. Acta Radiol 39:126-132, 1998.

30. Maffulli N, Regine R, Angelillo M, et al.: Ultrasound diagnosis of Achilles tendon pathology in runners. Br J Sports Med 21:158-162, 1987.

31. Kalebo P, Allenmark C, Peterson L, et al.: Diagnostic value of ultrasonography in partial ruptures of the Achilles tendon. Am J Sports Med 20:378-381, 1992.

32. Movin T, Kristoffersen-Wiberg M, Shalabi A, et al.: Intratendinous alterations as imaged by ultrasound and contrast medium enhanced magnetic resonance in chronic achillodynia. Foot Ankle 19:311-317, 1998.

33. Movin T. Aspects of aetiology, pathoanatomy and diagnostic methods in chronic mid-portion achillodynia [PhD]. Karolinska Institute, 1998.

34. Movin T, Gad A, Reinholt FP, et al.: Tendon pathology in long-standing achillodynia. Biopsy findings in 40 patients. Acta Orthop Scand 68:170-175, 1997.

35. Torstensen ET, Bray RC, Wiley JP: Patellar tendinitis: a review of current concepts and treatment. Clin J Sport Med 4:77-82, 1994.

36. Khan KM, Maffulli N, Coleman BD, et al.: Patellar tendinopathy: some aspects of basic science and clinical management. Br J Sports Med 32:346-355, 1998.

37. Karlsson J, Kalebo P, Goksor L-A, et al.: Partial rupture of the patellar ligament. Am J Sports Med 20:390-395, 1992.

38. Karlsson J, Lundin O, Lossing IW, et al.: Partial rupture of the patellar ligament. Results after operative treatment. Am J Sports Med 19:403-408, 1991.

39. Raatikainen T, Karpakka J, Puranen J, et al.: Operative treatment of partial rupture of the patellar ligament. A study of 138 cases. Int J Sports Med 15:46-49, 1994.

40. Colosimo AJ, Bassett FH: Jumper's knee: diagnosis and treatment. Orthopaedic Reviews 29:139-149, 1990.

41. Yu JS, Popp JE, Kaeding CC, et al.: Correlation of MR imaging and pathologic findings in athletes undergoing surgery for chronic patellar tendinitis. Am J Roentgenol 165:115-118, 1995.

42. King JB, Perry DJ, Mourad K, et al.: Lesions of the patellar ligament. J Bone Jt Surg 72-B:46-48, 1990.

43. Fritschy D, Wallensten R: Surgical treatment of patellar tendinitis. Knee Surg Sports Trauma Arthrosc 1:131-133, 1993.

44. Roels J, Martens M, Mulier JC, et al.: Patellar tendinitis (jumper's knee). Am J Sports Med 6:362-368, 1978.

45. Martens M, Wouters P, Burssens A, et al.: Patellar tendonitis: pathology and results of treatment. Acta Orthop Scand 53:445-450, 1982.

46. Ferretti A, Ippolito E, Mariani P, et al.: Jumper's knee. Am J Sports Med 11:58-62, 1983.

47. Cook JL, Khan K, Harcourt PR, et al.: A cross-sectional study of 100 cases of jumper's knee managed conservatively and surgically. Br J Sports Med 31:332-336, 1997.

48. Nichols CE: Patellar tendon injuries. Clin Sports Med 11:807-813, 1992.

49. Clancy WGJ. Tendon trauma and overuse injuries. In: Leadbetter WB, Buckwalter JA, Gordon SL, ed. Sports-induced inflammation: clinical and basic science concepts. Park Ridge, IL: American Academy of Orthopaedic Surgeons, 1990, 609-618.

50. Blazina ME, Kerlan RK, Jobe FW, et al.: Jumper's knee. Orthop Clin North Am 4:665-678, 1973.

51. Fritschy D, de Gautard R: Jumper's knee and ultrasonography. Am J Sports Med 16:637-640, 1988.

52. Myllymäki T, Bondestam S, Suramo I, et al.: Ultrasonography of jumper's knee. Acta Radiol 31(2):147-149, 1990.

53. Bodne D, Quinn SF, Murray WT, et al.: Magnetic resonance imaging of chronic patellar tendinitis. Skeletal Radiology 17:24-28, 1988.

54. Davies SG, Baudouin CJ, King JB, et al.: Ultrasound, computed tomography and magnetic resonance imaging in patellar tendinitis. Clinical Radiol 43:52-56, 1991.

55. Mourad K, King J, Guggiana P: Computed tomography and ultrasound imaging of jumper's knee - patellar tendinitis. Clinical Radiol 39:162-165, 1988.

56. Maffulli N, Regine R, Carrillo F, et al.: Ultrasonographic scan in knee pain in athletes. British Journal of Sports Medicine 26(2):93-96, 1992.

57. Cook JL, Khan KM, Harcourt PR, et al.: Patellar tendon ultrasonography in asymptomatic active athletes reveals hypoechoic regions: a study of 320 tendons. Clin J Sports Med 8:73-77, 1998.

58. Lian O, Holen KJ, Engebrestson L, et al.: Relationship between symptoms of jumper's knee and the ultrasound characteristics of the patellar tendon among high level male volleyball players. Scand J Med Sci Sports 6:291-296, 1996.

59. Khan KM, Cook JL, Kiss ZS, et al.: Patellar tendon ultrasonography and jumper's knee in elite female basketball players: a longitudinal study. Clin J Sports Med 7:199-206, 1997.

60. Khan KM, Cook JL, Bonar SF, et al.: Subcutaneous rupture of the Achilles tendon [letter]. Br J Sports Med 32:184-186, 1998.

61. Maffulli N, Waterston SW, Ewen SWB: Subcutaneous rupture of the Achilles tendon [letter]. Br J Sports Med 32:184-185, 1998.

62. Nirschl RP, Pettrone FA: Tennis elbow: The surgical treatment of lateral epicondylitis. J Bone Jt Surg 61-A:832-839, 1979.

63. Nirschl RP: Elbow tendinosis/Tennis elbow. Clin Sports Med 11:851-870, 1992.

64. Potter HG, Hannafin JA, Morwessel RM, et al.: Lateral epicondylitis: Correlation of MR imaging, surgical, and histopathologic findings. Radiology 196:43-46, 1995.

65. Ollivierre CO, Nirschl RP, Pettrone FA: Resection and repair for medial tennis elbow. A prospective analysis. Am J Sports Med 23:214-221, 1995.

66. Fukuda H, Hamada K, Yamanaka K: Pathology and pathogenesis of bursal side rotator cuff tears viewed from en bloc histologic sections. Clin Orthop 254:75-80, 1990.

67. Pettersson G: Rupture of the tendon aponeurosis of the shoulder joint in anterio-inferior disclocation: A study on the origin and occurrence of ruptures. Acta Chir Scand 87 suppl 77:1-184, 1942.

68. Nixon JE, DiStefano V: Ruptures of the rotator cuff. Orthop Clin North Am 6:423-447, 1975.

69. Kjellin I, Ho CP, Cervilla V, et al.: Alterations in the supraspinatus tendon at MR imaging: correlation with histopathologic findings in cadavers. Radiology 181:837-841, 1991.

70. Blevins FT, Djurasovic M, Flatlow EL, et al.: Biology of the rotator cuff tendon. Orthop Clin Nth Amer 28:1-16, 1997.

71. Wilson DL, Duff GL: Pathologic study of degeneration and rupture of the supraspinatus tendon. Arch Surg 47:121-135, 1943.

72. McLaughlin HL: Lesions of the musculotendinous cuff of the shoulder. III-Observations on the pathology, course and treatment of calcific deposits. Ann Surg 124:354, 1946.

73. Uhthoff HK, Sano H: Pathology of failure of the rotator cuff tendon. Orthop Clin Nth Amer 28:31-41, 1997.

74. Swiontkowski M, Iannotti JP, Boulas JH, et al. Intraoperative assessment of rotator cuff vascularity using laser Doppler flowmetry. In: Post M, Morrey BE, Hawkins RJ, ed. Surgery of the shoulder. St Louis: Mosby-Year Book, 1990,

75. Rathbun JB, McNab I: The microvascular pattern of the rotator cuff. J Bone Jt Surg 52-B:540-553, 1970.

76. Miniaci A, Dowdy PA, Willits KR, et al.: Magnetic resonance imaging evaluation of the rotator cuff tendons in the asymptomatic shoulder. Am J Sports Med 23:142-145, 1995.

77. Neumann CH, Holt RG, Steinbach LS, et al.: MR imaging of the shoulder. Appearance of the supraspinatus tendon in asymptomatic volunteers. Am J Roentgenol 158:1281-1287, 1992.

78. Mirovitz SA: Normal rotator cuff: MR imaging with conventional and fat-suppression techniques. Radiology 180:735-740, 1991.

79. Kaplan PA, Bryans KC, Davick JP, et al.: MR imaging of the normal shoulder: variants and pitfalls. Radiology 184:519-524, 1992.

80. Leadbetter WB: Cell-matrix response in tendon injury. Clin Sports Med 11:533-578, 1992.

81. Järvinen M, Jozsa L, Kannus P, et al.: Histopathological findings in chronic tendon disorders. Scand J Med Sci Sports 7:86-95, 1997.

82. El-Khoury GY, Wira RL, Berbaum KS, et al.: MR imaging of patellar tendinitis. Radiology 184:849-854, 1992.

83. Woo S-LY, Tkach LV. The cellular and matrix response of ligaments and tendons to mechanical injury. In: Leadbetter WB, Buckwalter JA, Gordon SL, ed. Sports-induced inflammation: clinical and basic concepts. Park Ridge, IL: American Academy of Orthopaedic Surgeons, 1990, 198-204.

84. Nirschl RP. Patterns of failed healing in tendon injury. In: Leadbetter WB, Buckwalter JA, Gordon SL, ed. Sports-induced inflammation: clinical and basic concepts. Park Ridge, IL: American Academy of Orthopaedic Surgeons, 1990, 577-585.

85. Enwemeka CS: Inflammation, cellularity, and fibrillogenesis in regenerating tendon: implications for tendon rehabilitation. Phys Ther 69:816-825, 1989.

86. Almekinders LC: Tendinitis and other chronic tendinopathies. J Am Acad Orthop Surg 6:157-164, 1998.

87. Kvist M, Jozsa L, Jarvinen M: Vascular changes in the ruptured Achilles tendon and its paratenon. Int Orthop 16:377-382, 1992.

88. Curwin S. The aetiology and treatment of tendinitis. In: Harries M, Williams C, Stanish WD, et al., ed. Oxford Textbook of Sports Medicine. Oxford: Oxford University Press, 1994.

89. Niesen-Vertommen SL, Taunton JE, Clement DB, et al.: The effect of eccentric versus concentric exercise in the management of Achilles tendonitis. Clin J Sports Med 2:109-113, 1992.

90. El Hawary R, Stanish WD, Curwin SL: Rehabilitation of tendon injuries in sport. Sports Med 24:347-358, 1997.

91. Sandmeier R, Renstrom P: Diagnosis and treatment of chronic tendon disorders in sport. Scand J Med Sci Sports 7:96-106, 1997.

92. Brukner P, Khan K. Clinical sports medicine. Sydney: McGraw-Hill, 1993.

93. Curwin S, Stanish WD. Tendinitis: its etiology and treatment. Lexington: Collamore Press, 1984

94. Vailas AC, Tipton CM, Laughlin HL, et al.: Physical activity and hypophysectomy on the aerobic capacity of ligaments and tendons. J Appl Physiol 44:542-546, 1978.

95. Zernicke RF, Garhammer J, Jobe FW: Human patellar-tendon rupture: a kinetic analysis. J Bone Jt Surg 59-A:179-183, 1977.

96. Clement DB, Taunton JE, Smart GW: Achilles tendinitis and peritendinitis. Etiology and treatment. Am J Sports Med 12:179-184, 1984.

97. Cannell LJ. The effects of an eccentric-type exercise versus a concentric-type exercise in the management of chronic patellar tendonitis. [Masters Thesis]. University of British Columbia, 1982.

98. Alfredson H, Pietila T, Jonsson P, et al.: Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. Am J Sports Med 26:360-366, 1998.

99. Kannus P, Jozsa L, Natri A, et al.: Effects of training, immobilization and remobilization on tendons. Scand J Med Sci Sports 7:67-71, 1997.

100. Reddy GK, Gum S, Stehno-Bittel L, et al.: Biochemistry and biomechanics of healing tendon: Part II. Effects of combined laser therapy and electrical stimulation. Med Sci Sports Exerc 30:794-800, 1998.

101. Fyfe I, Stanish WD: The use of eccentric training and stretching in the treatment and prevention of tendon injuries. Clin Sports Med 11:601-624, 1992.

102. Almekinders LC: The efficacy of nonsteroidal anti-inflammatory drugs in the treatment of ligament injuries. Sports Med 9:137-142, 1990.

103. Rolf C, Movin T, Engstrom B, et al.: An open, randomized study of ketoprofen in patients in surgery for Achilles or Patellar tendinopathy. J Rheumatol 24:1595-1598, 1997.

104. Astrom M, Westlin N: No effect of piroxicam on achilles tendinopathy. A randomized study of 70 patients. Acta Orthop Scand 63:631-634, 1992.

105. Vogel HG: Mechanical and chemical properties of various connective tissue organs in rats as influenced by non-steriodal antirheumatic drugs. Conn Tiss Res 5:91-95, 1977.

106. Weiler JM: Medical modifiers of sports injury: the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in sports soft tissue injury. Clin Sports Med 11:625-644, 1992.

107. Kennedy JC, Willis RB: The effects of local steroid injections on tendons: a biomechanical and microscopic correlative study. Am J Sports Med 4:11-21, 1976.

108. Shrier I, Matheson GO, Kohl HW: Achilles tendonitis: Are corticosteroid injections useful or harmful. Clin J Sports Med 6:245-250, 1996.

109. Anastassiades T, Dziewiatkowski D: The effect of cortisone on connective tissue in the rat. J Lab Clin Med 75:826-839, 1970.

110. Berliner DL, Nabors CJ: Effects of corticosteroids on fibroblast functions. Res J Reticuloendothel Soc 4:284-313, 1967.

111. Kapetanos G: The effect of local corticosteroids on the healing and biomechanical properties of the partially injured tendon. Clin Orthop 163:170-179, 1982.

112. Capasso G, Maffulli N, Testa V, et al.: Preliminary results with peritendinous protease inhibitor injections in the management of Achilles tendinitis. J Sports Traumatol Rel Res 15:37-43, 1993.

113. Capasso G, Testa V, Maffulli N, et al.: Aprotinin, corticosteroids and normosaline in the management of patellar tendinopathy in athletes: a prospective randomized study. Sports Exerc Injury 3:111-115, 1997.

114. Kvist M, Jarvinen M: Clinical, histochemical and biomechanical features in repair of muscle and tendon injuries. Int J Sports Med 3 Suppl 1:12-14, 1982.

115. Dow SM, Wilson AM, Goodship AE: Treatment of acute superficial digital flexor tendon injury in horses with polysulphated glycosaminoglycan. Vet Rec 139:413-416, 1996.

116. Sundqvist H, Forsskahl B, Kvist M: A promising novel therapy for Achilles peritendinitis: Double-blind comparison of glycosaminoglycan polysulfate and high-dose indomethacin. Int J Sports Med 8:298-303.

117. Rivenburgh DW: Physical modalities in the treatment of tendon injuries. Clin Sports Med 11:645-659, 1992.

118. Harvey W, Dyson M, Pond JB, et al.: The stimulation of protein synthesis in human fibroblasts by therapeutic ultrasound. Rheumatol Rehab 14:237-, 1975.

119. Enwemeka CS: The effects of therapeutic ultrasound on tendon healing. A biomechanical study. Am J Phys Med Rehab 68:283-287, 1989.

120. Jackson BA, Schwane JA, Starcher BC: Effect of ultrasound therapy on the repair of Achilles tendon injuries in rats. Med Sci Sports Exerc 23:171-176, 1991.

121. Snow CJ, Johnson KA: Effect of therapeutic ultrasound on acute inflammation. Physiotherapy Canada 40:162-167, 1988.

122. Enwemeka CS: Laser biostimulation of healing wounds: specific effects and mechanisms of action. J Sports Phys Ther 9:333-338, 1988.

123. Reddy GK, Stehno-Bittel L, Enwemeka CS: Laser photostimulation of collagen production in healing rabbit Achilles tendons. Lasers Surg Med 22:281-287, 1998.

124. Gum SL, Reddy GK, Stehno-Bittel L, et al.: Combined ultrasound, electrical stimulation and laser promote collagen synthesis with moderate changes in tendon biomechanics. Am J Phys Med Rehabil 76:288-296, 1997.

125. Astrom M, Arvidson T: Alignment and joint motion in the normal foot. J Orthop Sports Phys Ther 22:216-222, 1995.

126. Kamien M: A rational management of tennis elbow. Sports Med 9:173-191, 1990.

127. Lian O, Engebretsen L, Ovrebo RV, et al.: Characteristics of the leg extensors in male volleyball players with jumper's knee. Am J Sports Med 24:380-385, 1996.

128. Leadbetter WB, Mooar PA, Lane GJ, et al.: The surgical treatment of tendinitis: clinical rationale and biologic basis. Clin Sports Med 11:679-712, 1992.

129. Anderson DL, Taunton JE, Davidson RG: Surgical management of chronic Achilles tendinitis. Clin J Sports Med 2:38-42, 1992.

130. Coleman BD, Khan KM, Kiss ZS, et al.: Outcomes of open and arthroscopic patellar tenotomy for chronic patellar tendinopathy: a retrospective study. Am J Sports Med , (submitted).

131. Archambault JM, Wiley JP, Bray RC: Exercise loading of tendons and the development of overuse injuries. A review of the current literature. Sports Med 20:77-89, 1995.

132. Banes AJ, Tsuzaki M, Yamamoto J, et al.: Mechanoreception at the cellular level: the detection, interpretation, and diversity of responses to mechanical signals. Biochem Cell Biol 73:349-365, 1995.

133. Fukuda H, Hamada K, Nakajima T, et al.: Partial thickness tears of the rotator cuff. A clinicopathological review based on 66 surgically verified cases. Int Orthop 20:257-265, 1996.

134. Hamada K, Tomonaga A, Gotoh M, et al.: Intrinsic healing capacity and tearing process of torn supraspinatus tendons: in situ hybridization study of alpha 1 (I) procollagen mRNA. J Orthop Res 15:24-32, 1997.

135. Frank CB: Ligament healing: current knowledge and clinical applications. J Am Acad Orthop Surg 4:74-83, 1996.

136. Lee E, Maffulli N, Li CK, et al.: Pulsed magnetic and electromagnetic fields in experimental Achilles tendonitis in the rat: a prospective randomised study. Arch Phys Med Rehab 78:399-404, 1997.

137. Backman C, Boquist L, Friden J, et al.: Chronic Achilles paratenonitits with tendinosis: an experimental model in the rabbit. J Orthop Res 8:541-547, 1990.

138. Visentini PJ, Khan KM, Cook JL, et al.: The VISA score: An index of the severity of jumper's knee (patellar tendinosis). J Sci Med Sport 1:22-28, 1998.

139. Coleman BD. A comparison of outcomes of open and arthroscopic patellar tenotomy for patellar tendinopathy (jumper's knee): a retrospective study [BMedSci]. The University of Melbourne, 1998.

140. Kiss ZS, Kellaway D, Cook J, et al.: Postoperative patellar tendon healing - an ultrasound study. Australas Radiol 42:28-32, 1998.

141. Wiley JP, Bray RC, Wiseman DA, et al.: Serial ultrasonographic imaging evaluation of the patellar tendon after harvesting its central one third for anterior cruciate ligament reconstruction. J Ultrasound Med 16:251-255, 1997.

142. Khan KM, Visentini PJ, Cook JL, et al.: Open patellar tenotomy for jumper's knee: MR and ultrasound correlation with clinical outcome. Med Sci Sports Exerc 30, 1998.