Tendon Injury: A Review

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Abstract: This article describes the biomechanical and biochemical aspects of tendon anatomy and function, response of the tendon to injury, and factors contributing to injury. Clinical implications for treating patients with tendon injury are discussed.

Key Words: Tendon, Biochemical, Biomechanical, Injury, Anatomy, Function, Contributing Factors

Patients with tendon injuries are commonly referred to physical and occupational therapists. Traditionally, the term *tendonitis* has been used for virtually all painful afflictions of tendon structures, their synovial sheaths, and even adjacent bursae[1]. Mounting pathologic evidence, however, distinguishes between the acute traumatic inflammatory response of tendonitis and the more insidious process of chronic tendon degeneration[1]. This chronic degeneration is thought to be caused by overuse, and overuse tendon injuries are estimated to account for 30 to 50% of all sports-related injuries in the US[2,3]. Most industrial patients will also present with a slow insidious onset consistent with overuse tendon injuries.

This article provides the physical and occupational

therapist with the information necessary to make better informed treatment decisions for both acute, and chronic tendon injuries. We review tendon anatomy and function, response to injury, contributing factors to injury, and clinical relevance. This article is limited to issues related to the tendon midportion touching upon musculotendinous and osseotendinous junction issues only peripherally.

Anatomy

Tendons are usually found at the origin and insertion of a muscle. In some muscles, such as the rectus abdominis, they form tendinous intersections at the junctions of the original myotomes. Aponeuroses are large flattened tendons, usually composed of multiple layers, that can form major portions of a muscle[4]. As with all connective tissue structures, tendons are composed of a cellular and an extracellular component. Knowledge of the anatomy of the tendon is essential for understanding tendon biomechanics during normal function, injury, and

repair.

Fibroblasts are the main cellular component in all connective tissue structures[5]. In tendons, they are called *tenoblasts*[6] (the often used term tenocyte refers to a less metabolically active *tenoblast*[6]. A tenoblast has an enlarged rough endoplasmatic reticulum, a better developed Golgi-apparatus, and a larger amount of mitochondria than does a tenocyte[5]). All these adaptations are necessary to produce fibers, matrix or ground substance, cytokines, enzymes, and other proteins needed for the continuous turnover of the extracellular components[5].

Collagen fibers are the main extracellular component in tendons: they make up 70-80% of the dry weight[4,5,7]. The structural unit of collagen is tropocollagen, a protein some 280 nm long and 1.5 nm wide[4]. Tropocollagen is formed from procollagen when the non-helical peptides at both ends of a procollagen molecule are enzymatically removed after it exits the tenoblast[4]. A tropocollagen molecule consists of three helically-arranged polypeptide or alpha-chains[5]. Polypeptide chains are made up of linked amino-acid residues. Unique to the alpha-chains in tropocollagen is that every third position is occupied by the amino-acid residue glycine[4,5]. Proline (12%), hydroxyproline (10%), lysine, and hydroxylysine are the other major components of the alpha-chains[4,5]. Figure 1 illustrates the amino-acid residue sequence in the alpha-chains and the integration of the alpha-chains into, ultimately, the collagen fibril. The three polypeptide chains in tropocollagen are stabilized by intramolecular hydrogen bonds (Fig. 2). Hydrogen bonds are electrostatic bonds between molecules[5]; hydrogen residues in glycine form these intramolecular cross-links with the carboxyl (-COOH) groups of proline in adjacent chains[5]. The tropocollagen molecule is further stabilized by the hydrogen bonds between the hydroxyl (-OH) groups in the hydroxylysine residues[5]. Covalent bonds are chemical bonds in which two molecules share a number of mutual electrons[8]. Some lysine and hydroxylysine residues will trade a methylamine group ($-CH2NH2$)[8] for an aldehyde group (-HC=O) (Fig.3); in turn these highly reactive aldehyde groups will form covalent intramolecular cross-links with aldehyde groups from the adjacent alpha-chain[5]. Once outside the tenoblast, four or five tropocollagen molecules aggregate into microfibrils[5,7] (Fig.1); each microfibril is approximately 4 nm in diameter[7]. The tropocollagen molecules in the microfibrils overlap each other by a quarter, which causes the cross-striated appearance of collagen fibers[4]. Variable numbers of these microfibrils aggregate to form collagen fibrils: the diameters of these fibers, therefore, vary between 30 and 400 nm[7]. Fibrillogenesis or organization of tropocollagen molecules into microfibrils and fibrils results from covalent intermolecular cross-linking between aldehyde groups of lysine and hydroxylysine residues in adjacent fibrils, similar to the intramolecular crosslinks described earlier[5]. Fibrils further organize in the form of fibers, and
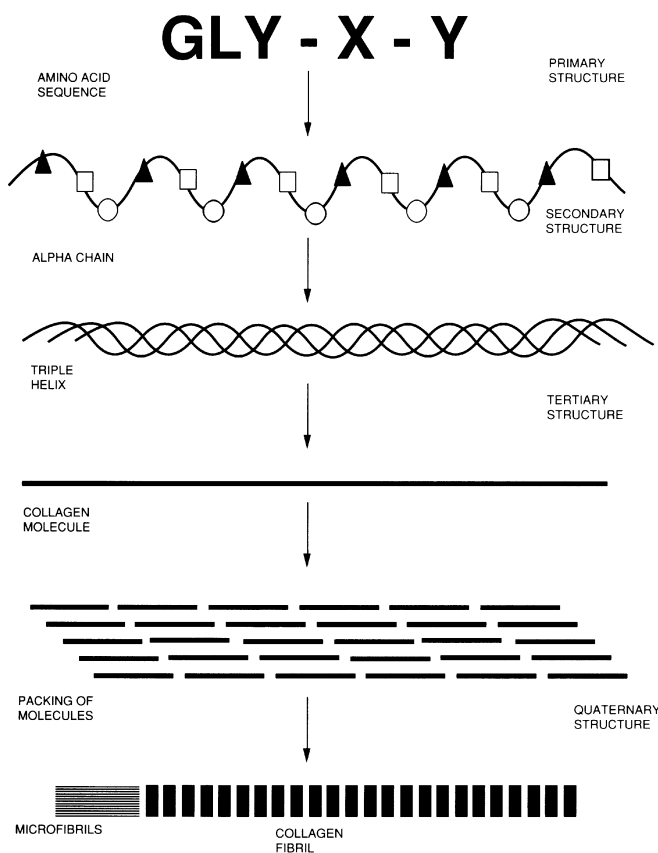

Fig. 1: Molecular structure of collagen (from Van Wingerden BAM. Connective Tissue in Rehabilitation, Vaduz Liechtenstein, Scipro Verlag, 1995, fig. 8; pg. 27).
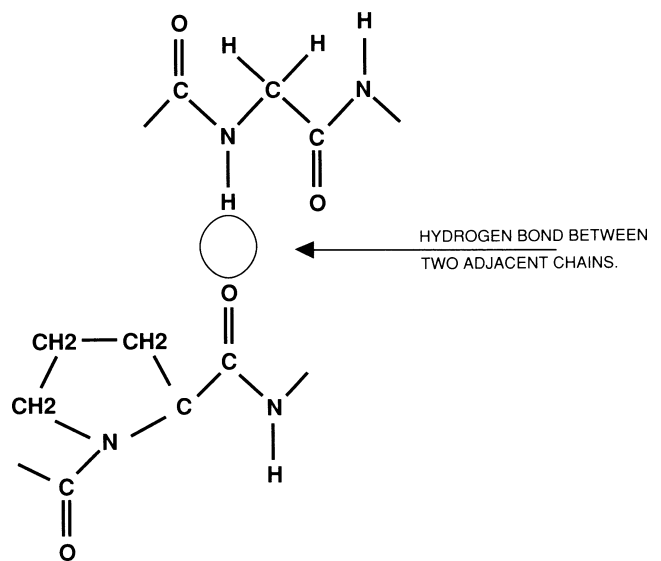

Fig. 2: Hydrogen bond (from Van Wingerden BAM. Connective Tissue in Rehabilitation, Vaduz Liechtenstein, Scipro Verlag, 1995, fig. 7; pg. 26).

groups of parallel fibers in turn form fascicles[2]. In tendons subject to forces in multiple directions, fascicles are interwoven without regular orientation, while tendons subject to tensile forces in mainly one direction have an orderly arrangement of parallel fascicles[4]. The space between the individual fibers is thought to be too large for cross-links to form, except possibly in cases of immobilization with a decreased interfiber distance. Ground substance, the other major extracellular component, plays the main role in aggregation from the fibril level up[7].

Ground substance, like collagen, is produced by the tenoblasts. It is an aqueous gel-like solution of glycosaminoglycans, proteoglycans, and glycoproteins, surrounding the collagen fibers and tenoblasts[4]. Ground substance is the medium for diffusion of gases, nutrients, and metabolites to and from the metabolically active tenoblasts[4]. Glycosaminoglycans (GAGs) are linear polysaccharides or linked-sugar chains formed by repeating disaccharide units[5,6]. Examples of GAGs in human connective tissues are hyaluronic acid, chondroitin-4-sulphate, chondroitin-6-sulphate, dermatan sulphate, and keratan sulphate[5] (Table 1). Chondroitin-6- and dermatan sulphate are the GAGs most frequently found in tendons[5]. When connected to a core protein, multiple GAGs form a proteoglycan molecule[5,6]. GAGs are extremely hydrophilic: even though they make up only one percent of the dry tissue weight of a tendon they bind water for up to 65-75% of the total tendon weight[7]. This water-binding capacity of GAGs is the result of negative charges on their many carboxyl, hydroxyl, and sulphate groups, which form electrostatic bonds with water molecules[5]. Negative charges of adjacent GAGs in a proteoglycan molecule will also repulse one another causing the proteoglycan molecule to occupy a maximal volume[5,6]. Collagen fibers contain multiple positively-charged groups and interaction with the negatively-charged groups of the GAGs and proteoglycans is responsible for organizing fibrils into fibers and fascicles[6,7]. These electrostatic interactions also play a role in restoring collagen fibers to their starting position after tensile force

on the tendon is released[6]. Under normal circumstances, GAGs and proteoglycans prevent interfibrillar cross-linking by maintaining interfibrillar and interfiber distance[5]. Proteoglycans and GAGs also appear to play a role in determining fibril diameter: larger concentrations of GAGs and proteoglycans are correlated with smaller diameter fibrils[7], and proteoglycan content decreases as fibrils reach their ultimate size[4]. Fibronectin is the most important glycoprotein or carbohydrate-protein combination[5]. Fibronectin binds the fibroblasts to the collagen fibers[4] and is important in guiding the proliferation of new collagen during healing[5].

Elastin is the other fiber type in tendons: collagen accounts for 30% of the wet tendon weight, elastin only for 2%[4]. Elastin is composed mainly of the amino-acid residues glycine, proline, alanine, and valine[4,5]; it contains little hydroxyproline and no hydroxylysine[5]. The polypeptides in elastin fibers have no periodicity: there is no repetition as in the alpha-chains of tropocollagen where glycine occupies every third position[4,5]. Tropoelastin molecules form covalent bonds with other tropoelastin molecules to form elastin fibers: the structure of elastin fibers allows 70% elongation without fiber disruption[4]; complete failure only occurs at 150% elongation[4] (Fig. 4). Elastin contributes to the elasticity of the tendon[4].

Loose areolar connective tissue sheaths surround the tendon fibers at different hierarchical levels. Groups of fibers are surrounded by a sheath called the endotenon, thus forming fascicles. This endotenon consists mainly of small-diameter type-III collagen fibrils[7]. In addition to allowing movement between fascicles, the endotenon carries blood and lymph vessels and nerves[3,7]. The epitenon surrounds the entire tendon; its inner surface blends with the endotenon of the fascicles[3]. The epitenon can be differentiated from the endotenon as it consists of larger-diameter mainly type-I collagen fibers[7]. An additional double-layered tissue sheath, called the paratenon, is loosely attached to the outer surface of the epitenon[7] and functions as an

$$R$$
$$|$$
$$C = O$$
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$$C - (CH_2)4 - NH_2 \quad \xrightarrow{\textit{LYSYL OXIDASE}} \quad C - (CH_2)3 - C = O$$
$$| \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad | \qquad\qquad\qquad\quad H$$
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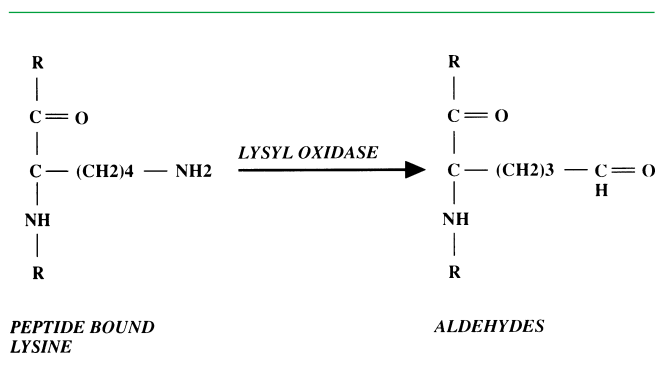
PEPTIDE BOUND LYSINE   ALDEHYDES

Fig. 3: Acquiring aldehyde groups (from Van wingerden BAM. Connective Tissue in Rehabilitation, Vaduz Liechtenstein, Scipro Verlag, 1995, fig. 18; pg. 35).
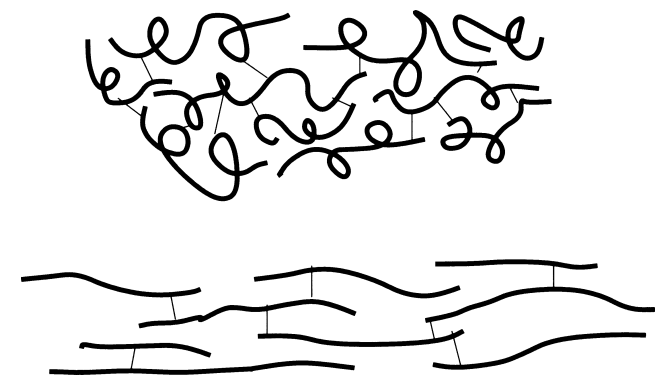
Fig. 4: Elastic properties of elastin (from Van wingerden BAM. Connective Tissue in Rehabilitation, Vaduz Liechtenstein, Scipro Verlag, 1995, fig. 22; pg. 39).

Table 1. GAGs in Human Tissues (from Van wingerden BAM. Connective Tissue in Rehabilitation, Vaduz Liechtenstein, Scipro Verlag, 1995; fig. 29; pg. 43)

GLYCOSAMINOGLYCANS IN THE DIFFERENT TISSUES	
HYALURONIC ACID	BASIC CHAIN OF PROTEOGLYCANS IN MANY TISSUES AS CARTILAGE, BUT ALSO AS SEPERATE GAG IN SKIN, SYNOVIA ETC.
CHONDROINTIN 4 SULFATE	CARTILAGE, BONE, INSERTIONS TO BONE, SKIN ETC.
CHONDROINTIN 6 SULFATE	CARTILAGE, TENDON, DISCUS ETC.
DERMATAN SULFATE	SKIN, TENDON, LIGAMENTS, CAPSULE, FASCIA
KERATAN SULFATE	CARTILAGE, BONE, DISCUS ETC.

elastic sleeve allowing free movement of the tendon against the surrounding tissue[3]. The epitenon and paratenon together compose the peritenon[3]. In areas of friction, the paratenon develops into a true synovial sheath consisting of two concentric layers separated by a film of synovial fluid: the visceral layer surrounds the tendon, the parietal layer is attached to the adjacent connective tissue[4] (Fig. 5). Inflammation can cause cellular proliferation and increased production of synovial fluid in the synovial sheath which may result in adhesions restricting motion between the two layers[4].

The blood supply of tendons can be divided into three regions[4]. The supply to the musculotendinous junction is from the superficial vessels in the surrounding tissues: small arteries branch and supply both muscle and tendon; however, they do not form anastosmoses[4]. Vessels supplying the bone-tendon junction take care of the lower third of a tendon; again, the vessels between bone and tendon do not anastosmose due to the fibrocartilaginous barrier[4]. The blood supply to the tendon midportion is via the paratenon: vessels in the paratenon run transversely into the tendon, branch multiple times, and then enter the endotenon to run parallel to the long axis of the tendon[4]. In tendons with a synovial sheath, a thin sheath called the *mesotendineum* bridges the synovium-filled space to the epitenon containing blood and lymph vessels[6] (Fig. 5). In the flexor tendon sheaths of hand[4,6] and foot[4], there is no mesotendineum over the whole length of the synovial sheath but rather a distinct number of narrow bridges called *vinculae* containing such vessels[6]. In tendons with a synovial sheath, diffusion through the synovial fluid also plays a role in the nutrition of the tenoblasts[6]. Tendon vascularity tends to be very irregular especially mid-substance and in areas where the tendon is twisted or follows a bony prominence[9]. This may play a role in tendon pathology.

Function

The mechanical behavior of tendons can be visualized by a force-elongation curve (Fig. 6). To produce this curve, a tendon specimen is subjected to tensile deformation using a constant rate of elongation until the tissue ruptures; the resulting force is plotted against the elongation produced[10]. A stress-strain curve is a very similar curve with slightly different parameters being measured: strain (the deformation of the tissue calculated as a percentage of the original length of the specimen[10]) is plotted on the horizontal axis against stress (force per unit area[10]) on the vertical axis. Force-elongation and stress-strain curves have four regions: the toe region, the linear region, the region of microscopic failure, and the region of macroscopic failure[2].
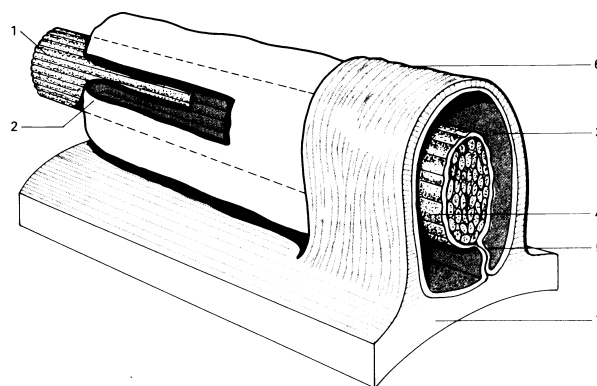

Fig. 5: Structure of tendon with a synovial sheath (1. tendon; 2. fold connecting visceral and parietal layer; 3. parietal layer; 4. visceral layer; 5. mesotendineum; 6. vagina fibrosa tendinis; 7. bone) (De Morree JJ. Dynamiek van het Menselijk Bindweefsel. 2nd ed. Houten, The Netherlands: Bohn Stafleu Van Loghum, 1993. fig. 6.10; pg. 123).
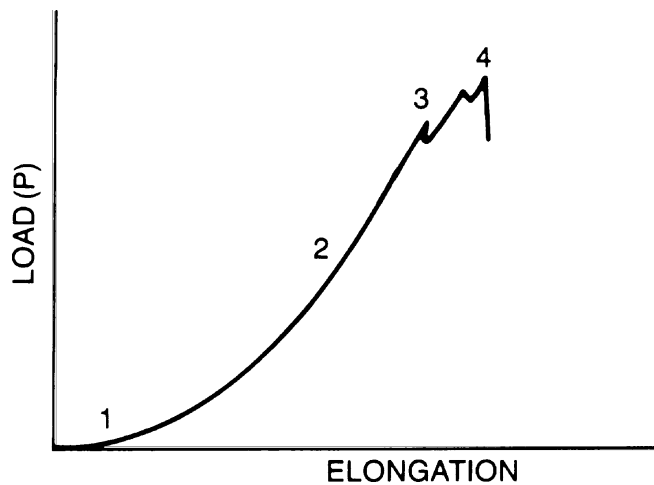
Fig. 6: Load-elongation curve (Nordin M, Frankel VH. Basic Biomechanics of the Musculoskeletal System. 2nd ed. Philadelphia, USA: Lea & Febiger, 1989, fig. 3.5; pg. 63).

The collagen fibers in normal, unloaded tendons have a wavy configuration[3] maintained by the electrostatic interaction between the negative charges on the GAG molecules and the positively-charged collagen molecules[6]. The initial response to tensile forces is a straightening of the collagen fibers with the wavy configuration disappearing at 2% elongation[3]. Little force is required for rapid changes in length in this toe region of the force-elongation curve, but there is little or no physical deformation of collagen fibers[7]. The ground substance is responsible for resisting tensile forces in this region[6].

Application of tensile stresses beyond the toe region directly load the collagen fibers with a linear relationship between applied force and elongation increments[7]; this part of the curve between 2 and 4% elongation is therefore called the linear portion[2]. The modulus of elasticity, calculated by dividing stress by strain, gives us a numerical value for the stiffness of the tendon tissue in this region[10]. Mechanical behavior of the tendon is determined by structural and material properties. Structural properties are size-dependent features: length, number of fibers oriented in the direction of the stress applied, and cross-sectional area[2,7]; material properties are features related to tendon composition: amount and type of collagen, and number and type of cross-links[7]. As examples for the effect of material properties: type-III collagen found in healing tendon tissue has less tensile strength than type-I collagen found in mature healthy tendons[1], and electrostatic bonds will fail sooner than covalent cross-links in response to mechanical loading[11].

At the end of the linear region, small dips can sometimes be observed in a stress-strain curve; this point where the curve starts to level off towards the strain or elongation axis is called the yield point[10]. Microscopic failure occurs between 4 to 8% strain[2-4]: collagen fibers start to slide past one another as cross-links start to fail; and as more and more cross-links are broken, the weakest fibers will rupture at a microscopic level[4]. Successive failure of collagen fibers and fibrils will lead to a plateau in the stress-strain curve: this point represents the ultimate tensile strength of the tendon[10]. The drop-off in the curve after this point between 8 to 10% elongation is caused by macroscopic disruption of the tendon structure up to complete rupture[2].

Tendons are viscoelastic structures[4], so their mechanical behavior is not only determined by structural and material properties, but also by the rate at which they are loaded[3,10]. The linear portion of the stress-strain curve becomes steeper with increased strain rates: the tendon becomes stiffer when the load is applied more rapidly[10]. Ultimate tensile strength also increases with higher strain rates[10], allowing for more storage of elastic energy in the tendon during a stretch-shortening cycle (movement in which a phase of rapid eccentric action precedes a concentric contraction of the same muscles, e.g. throwing, walking, and jumping). During such a cycle, in the eccentric phase, elastic energy is stored in the connective tissue structures of a muscle to be released during the concentric phase. More important in explaining tendon pathology is viscoelastic tendon behavior under prolonged or repeated loading situations. Prolonged application of a constant load will lead to an increase in elongation over time, a phenomenon known as *creep*[10,11]. When this elongation extends into the region of microscopic failure, it may result in plastic deformation or disruption of the tendon tissue. Repeated loading will displace the force-elongation curve to the right: the same force will produce a bigger elongation after multiple loading cycles[10]. Repeated loading will also increase the slope of the linear region indicating an increase in stiffness[10]; this causes microfailure to occur at stresses normally within a physiologic range when they are applied to a tissue which has been exposed to cyclic loading previously[10].

Biochemical and biomechanical response to injury

Tendon injury can be defined as a loss of cells or extracellular matrix caused by trauma[1]. Injury represents a failure of cell and matrix adaptation to load exposure. This load exposure can be sudden, leading to acute trauma, or it can be repeated or prolonged, leading to overuse trauma. Either way, tendon injury will initiate attempts at repair, defined as replacement of damaged or lost cells and extracellular matrices by new cells and matrices[1]. Repair occurs through the inflammatory process, a localized tissue response initiated by injury or destruction of vascularized tissues exposed to excessive mechanical load or use[1]. The inflammatory process has three phases:

the acute vascular-inflammatory phase, the repair-regeneration phase, and the remodelling-maturation phase[1].

In the acute vascular-inflammatory phase, the glycoprotein fibrin contained in the fibrin clot cross-links with collagen to provide the initial wound strength. Platelets at the injury site are the source of multiple cell mediators, such as platelet-derived growth factor (PDGF), platelet factor 4, insulin-like growth factor (IGF)1, transforming growth factor (TGF) beta-1 and -2, and an uncharacterized chemotractant for endothelial cells. PDGF stimulates polymorphonuclear leukocyte migration into the extravascular space. Polymorphonuclear leukocytes are also known as neutrophils[12]; these cells produce the proteases collagenase and elastase, which break down collagen and elastin fiber debris. They also initiate the chemotaxis of other inflammatory cells. Hyaluronate, a high molecular weight GAG, interacts with fibronectin to form a scaffold used in this cell migration[1]. Neutrophils extend pseudopodia around debris; these pseudopodia fuse around the debris closing them into vacuoles, called phagosomes, inside the cell. Granules within the neutrophil fuse with the phagosome to discharge their content of hydrolytic enzymes into the phagosome[12]. These hydrolytic enzymes start hydrolyzing cell membrane phospholipids, producing arachidonic acid. The resulting series of chemical reactions called the arachidonic acid cascade produces prostaglandins, eicosanoids, leukotrienes, thromboxanes, and slow-reacting substance of anaphylaxis (SRS-A). These substances are responsible for the cardinal signs of inflammation, which usually last 3-5 days provided there is no further disturbance to the damaged area[1]. Neutrophils can function with a mainly anaerobic metabolism[12]; during phagocytosis, however, there is a temporary increase in oxygen consumption, which leads to the formation of hydrogen peroxide ($H2O2$) and superoxide anions ($O2-$). This superoxide anion is a short-lived free radical formed by adding one electron to an oxygen molecule; it is highly reactive and aids in destruction of cellular debris ingested by the neutrophil[12].

The repair-regeneration phase is also known as the fibroblastic-proliferative phase[2] and is characterized by the presence of the tissue macrophage[1]. These macrophages differentiate from circulating monocytes after entering the extravascular space[12]; they are capable of releasing growth factors, chemotractants, and proteolytic enzymes as needed for tenocyte activation[1]. Macrophage-derived growth factor and TGF-beta cause proliferation of tenoblasts thought to originate in the epitenon[11]. The tenoblasts rapidly produce type-III collagen, which is characterized by smaller fibrils lacking cross-links, therefore lacking tensile strength. Later in this phase, the fibroblasts shift to producing type-I collagen. Initially there are no cross-links between the tropocollagen molecules[2,4]: this facilitates enzymatic breakdown and reorganization[4]. Cross-links start to develop at 6-14 days post-injury increasing tensile strength to the area of injury[2,4]. Collagen fibril deposition is haphazard at first , but later the fibrils come to lie parallel to tensile forces within the tissue[2,4]. This phase lasts from approximately 48 hours to 6-8 weeks post-injury[1].

In the remodelling-maturation phase, cellularity and synthetic activity decreases in the tendon (even after 84 days, however, collagen production has been shown to be 15 times that of normal[4]). The extracellular matrix becomes more organized: functional linear realignment is usually restored by two months after the initial tendon injury. The collagen is matured, which means increased cross-linking, as well as decreased type-III and increased type-I collagen content. Injured tendon tissue, however, may only regain 70-80% of its original structural and biomechanical integrity as long as a year post-injury[1].

Factors contributing to injury

The most basic concept in the etiology of tendon injury is that the tendon is exposed to forces that damage it[7]. Damage can result from forces that cause elongation of the tendon tissue extending into the micro- and macrofailure region. Under physiological circumstances, tendons function in the toe and linear region of the stress-strain curve. However, *in vivo* studies (e.g. with buckle transducers on the Achilles tendon) in humans have shown loads close to and exceeding damaging forces as estimated based on *in vitro* measurements[7]. Even though measurement inaccuracies with *in vivo* buckle transducer measurements must be considered because of indirect calibration and the highly invasive nature of the transducer implantation[9], clearly eccentric muscle action with simultaneous application of maximum force and maximum elongation on the tendon can generate sufficient force to cause damage[7].

Muscles determine the magnitude of strain in their tendons by absorbing energy from repetitive shocks and stresses. Fatigue decreases muscle contractility and increases strain to the tendon. Improper warming-up impairs muscle enzyme function, contractility and the ability to absorb shocks[3].

As discussed earlier, repeated and prolonged load application has been shown to alter the stress-strain curve of tendon tissue: tendon injury may result from repeated loading into what would normally be the higher linear region of that curve[7]. Rapid unloading has also been associated with tendon injury: sudden force release is hypothesized to break interfibrillar adhesion because of shearing forces within the tendon[7].

Therefore, tendon injury can be caused by forces that are too big for the tissue to withstand. The tendon can also change so that "normal" forces now cause injury; these changes can occur through genetic disorders, aging, vascular changes, endocrine influences, nutritional deficiencies, inactivity, immobilization, and exercise[1,3,4,7,9,13].

Genetic disorders may affect connective tissue mor-

phology and, therefore, its mechanical properties. For example, in Ehlers-Danlos syndrome, decreased cross-linking leads to weaker tendon tissue that elongates more rapidly with force application[7].

Aging also affects connective tissue morphological and mechanical characteristics. With increasing age, tendon collagen content increases, while elastin and proteoglycan content decrease; water content decreases from 80% at birth to 30% in old age[3,13]. The number of irreducible cross-links also increases with age[1,4]. Mechanically, this translates into a less elastic, less compliant tendon, more prone to shear injury[1,13]. Aging tenocytes show a decrease in the intracytoplasmic organellae responsible for protein synthesis[1]. Because of the increase in density and aggregation of the extracellular matrix with age as a result of the decreased water and increased collagen content, the permeability of the matrix affecting nutrition to the tenocytes is altered[4]; decreasing tendon vascularity, as shown in the Achilles tendon after the third decade of life[13], may further decrease tenocyte nutrition. Metabolic pathways used by the tenocytes and tenoblasts for energy production change from aerobic to more anaerobic, eventually shutting down some pathways such as the Krebs cycle[3,13]; this decreases collagen turnover and fibroblastic activity, negatively influencing the repair capabilities of aging tendon tissue. The combined effect of less compliance and decreased repair ability may make aged tendon tissue more prone to injury[3].

Endocrine factors also influence tendon anatomy and function. Increased cross-linking is more likely in diabetics, resulting in stiffer tendons[7]; microangiopathy with resulting decreased circulation may cause this increase. Endocrine responses to stress and overtraining include an increased release of catecholamines (epinephrine and norepinephrine); these substances increase collagen turnover and decrease cross-linking[7]. Glucocorticoids are catabolic substances inhibiting the production of new collagen[4]. Insulin, estrogen, and testosterone can increase collagen production[4]: diminished estrogen levels, premature menopause, and premenopausal hysterectomy may predispose women to chronic tendon injury[1].

Nutritional deficiencies of cofactors important in collagen synthesis and cross-linking (vitamines A and C and copper) may affect tensile strength of tendons[7]. This may play a role in tendon injuries in the sometimes nutritionally deficient elderly patient.

Inactivity and immobilization result in increased collagen degradation, decreased tensile strength, and decreased concentration of metabolic enzymes in tendons[4], exercise, on the other hand, increases collagen synthesis, number and size of fibrils, concentration of metabolic enzymes, and tensile strength of tendons[4]. There is evidence from animal research, however, that there may be a transient period of mechanical weakness following exercise with increased collagen turnover, decreased mature cross-link content, and decreased GAG concen-tration[9].

Kannus and Joszpa[13] did histopathological analyses on 891 spontaneously ruptured tendon samples taken during surgical repair within 48 hours of rupture. They compared these tendon specimens to 445 age-and sex-matched controls taken within 24 hours of the time of accidental death from previously healthy individuals. A healthy structure was absent in all spontaneously ruptured tendons, whereas two-thirds of the control tendons were structurally healthy. Most pathologic changes (97%) were degenerative in nature. Hypoxic degenerative tendinopathy was found in 44% of the ruptured tendons: these specimens showed alterations in the shape and size of mitochondria and nuclei of the tenocytes with occasional intracytoplasmic or mitochondrial calcification. In advanced-stage specimens, tenocytes had hypoxic or lipid vacuoles and there was occasional tenocyte necrosis. Collagen fiber abnormalities included longitudinal splitting, disintegration, angulation, and variations in fiber diameter. Mucoid degeneration was found in 21% of specimens: large mucoid patches and vacuoles filled with GAGs and proteoglycans had accumulated between thin and fragile collagen fibers. The cytoplasm of the tenocytes was filled with dilated vacuoles and degranulated endoplasmatic reticulum. In 8% of ruptured tendons, there was evidence of tendolipomatosis: lipid cells had accumulated between collagen fibers; in advanced stages three-dimensional conglomerations of lipid cells caused disruption and atrophy of collagen fibers. Calcifying tendinopathy, found in 5% of specimens, was characterized by large deposits of calcium between or on degenerated and fragile collagen fibers; in 22% of ruptured tendons, evidence of multiple forms of degeneration existed. In 62% of the ruptured tendons, there was narrowing or even obliteration present of the lumen of arteries and arterioles in the tendon and paratenon due to hypertrophic changes in the tunica intima and media; 16% showed evidence of proliferative arteriitis and arteriolitis. These vascular changes were also present in two-thirds of that portion of control tendons that did show evidence of degenerative changes.

Decreased blood flow has been implicated most frequently to explain hypoxic degenerative tendon changes[4]. The decrease in blood flow may diminish the capacity to supply the tenocytes with oxygen and nutrients and to remove metabolites. Mature tenocytes depend partly on an oxidative metabolism making them sensitive to tissue hypoxia[9]. As discussed previously, blood supply to the tendon is usually irregular in the tendon midportion and in places where the tendon is twisted or follows a bony prominence[9]; decreased vascularity has been shown in the Achilles tendon 4 cm proximal to its calcaneal insertion and in the posterior tibial tendon just distal and posterior to the medial malleolus[9]. Areas of hypovascularity have also been found in the supraspinatus tendon 1 cm from its insertion, in the superior portion of the infraspinatus near its insertion, and in the intracapsular segment of

the tendon of the long head of the biceps brachii when stretched over the head of the humerus[4]. Hypovascularity is also hypothesized to play a major role in calcifying tendinopathy[13]: persistent hypoxia in a poorly vascularized portion of the tendon may transform some of the tenoblasts into chondroblasts able to function under anaerobic circumstances. These chondroblasts can cause depositing of calcium at multiple places throughout the tendon.

Hypovascularity may also play a role in two other hypotheses on the etiology of tendon degeneration. Certain areas of a tendon may be subjected to transient ischaemia during exercise as a result of anatomically-determined regional hypovascularity. Subsequent reperfusion has been shown to involve oxygen-derived free radicals. As discussed earlier, these highly reactive molecules play a role in phagocytosis; they are also capable of tissue destruction leading to degenerative tendon changes[9]. Tendons not only transmit forces from muscles to bones, but they also act as elastic energy stores during stretch-shortening cycles[14]. During cyclic loading, not all elastic energy stored in the tendon is recovered on unloading: some 5-10% is released as heat. A good blood supply will cool overheated tissue, but in hypovascular regions of the tendon, this protective mechanism may be insufficient, and the thermal energy released may cause hyperthermic damage to tendon cells and collagen[14]. Wilson and Goodship[14] implanted thermosensors in superficial flexor digitorum tendons of racehorses galloping at 9.3-10.5 m/s for 5 minutes. Mean peak temperature in the central core of the tendon was found to be 43.4+/-.9°C. The highest core temperature recorded was 45.4°C. Heating above 42°C has been shown *in vitro* to damage some types of fibroblasts; *in vivo* cell damage will occur with heating over 42-43°C[14].

Clinical implications

To summarize the above information: healthy tendons get injured either by a single application of force sufficient to cause tissue disruption, or by repeated or sustained force applications that alter the mechanical characteristics of the tendon so that forces that normally would fall within the safe range now cause tissue injury. Genetic disorders, aging, decreased vascularity, endocrine influences, nutritional status, inactivity, immobilization, and exercise may cause tendon degeneration, thus rendering the tendon more susceptible to injury when force is applied. Hypovascularity is hypothesized to play the major role in this degeneration, both directly by causing an ischaemic environment for the fibroblast and indirectly both by contributing to the production of free radicals and by allowing for tissue hyperthermia to occur.

Treatment of tendon injuries should always have two components: remove or decrease the forces leading to the injury and change the morphological and mechani-

cal characteristics of the tendon so that these forces are no longer injurious. Forces damaging a tendon can be external such as ill-fitting shoes, concrete work floors, and work equipment requiring high forces or excessive range of motion. In work-related injuries, ergonomic analysis of the work place is needed. In sports-related tendon injuries, analysis of technique and equipment is necessary. Internal forces on the tendon result from interaction with adjacent structures of the musculoskeletal system. A thorough evaluation should focus on contributing or causative impairments, such as capsuloligamentous hyper- or hypomobility, myofascial restrictions, decreased strength and endurance, and neuromuscular dyscoordination.

When dealing with tendon injuries, physical and occupational therapists may use mechanical, thermal, and chemical stimuli to affect the morphological and mechanical characteristics of the tendon and to influence progression of the inflammatory process. The role of modalities and medications (e.g., iontophoresis) lies outside the scope of this article. However, when using mechanical forces, the therapist should first establish the phase of the inflammatory process. During the vascular-inflammatory phase, tissue protection is needed, but a progressive regimen of physiological tensile forces adapted to the stage of healing will help restore fibrillar alignment, appropriate crosslinking, and normal mechanical properties during subsequent phases. This same progressive tensile-loading program may also be instrumental in primary and secondary prevention of tendon injuries.

One problem with this management strategy is how to identify the current phase of the inflammatory process within the injured tendon. Acute traumatic tendon injuries may present with a clear time of onset, but overuse tendon injuries usually have an insidious onset, making it impossible to establish when the inflammatory process started. Continuous reinjury, as is common with overuse injury, will repeatedly set back the progression of the inflammatory process. We discussed earlier how certain factors may contribute to tendon injury. It is unclear how these factors affect the normal time frames of the different phases of the inflammatory process. We must realize that our knowledge of the "normal" inflammatory process and duration of its phases is based on data collected from complete tendon lacerations; little is known about the inflammatory response to the type of mechanical trauma that causes chronic tendon injuries[7]. A good patient history should at least focus on establishing the presence of the factors possibly contributing to injury. Assuming that any tendon injury, unless proven otherwise, is in the vascular-inflammatory phase and to act accordingly may be a sound clinical decision.

Another problem lies in assuming that chronic tendon injuries are simply recurrent acute tendon injuries. Kannus and Josza[13] showed degenerative changes in spontaneously ruptured tendons that were obviously not consistent with the normal inflammatory process described

earlier. In chronic tendon injuries, the infiltration of inflammatory cells and the orderly phased repair process seem either absent or cut short[1,13]; this finding has led to a new system of classification for tendon injuries (Table 2)[1]. Based on the anatomy of tendon and peritenon, this classification describes four different pathologic conditions, which distinguish between involvement of peritenon/synovial sheath and/or involvement of the tendon itself. This classification system also reflects the type of adaptation to injury taking place within the tendon: the term *tendonitis* is reserved for tendon substance changes with evidence of inflammation, whereas the term *tendinosis* describes a focal area of intratendinous degeneration that is initially asymptomatic[1]. Histologic findings in tendonitis, tendinosis, and paratenonitis are also mentioned in Table 2. Characteristic of tendinosis is its non-inflammatory nature. Some authors argue that tendinosis develops without any associated inflammation in tendon or tendon sheath[7]; on the other hand, tendinosis may represent only the late fibrotic stage of tendonitis, not excluding an earlier presence of inflammatory symptoms[7]. It is unclear whether tendonitis, tendinosis, and paratenonitis will respond similarly to the application of therapeutic stimuli.

The classification system presented in Table 2 is based on histologic findings and clinical signs and symptoms. Once research helps establish the most appropriate treatment approaches for these different conditions, this system may prove extremely useful. However, due to the therapist's scope of practice, diagnosis and classification will be determined based on clinical findings. Referring to tendon injury, Leadbetter stresses that elicitation of pain does not necessarily shed light on the exact nature of the pathology[1]. For example, two-thirds of the patients in the study by Kannus and Josza[13] experienced no symptoms prior to their spontaneous tendon rupture. Tendinosis is per definition initially asymptomatic[1]. Good history-taking and the use of common sense-based clinical reasoning to find out about the presence of repeated or prolonged symptoms of tendon or peritenon injuries may be more important in confirming suspected tendinosis than the results of actual tests during physical evaluation.

The final problem with the management strategy discussed above deals with applying a progressive regimen of tensile forces to strengthen the tendon both in order to rehabilitate it after injury, and to prevent tendon injury. Research shows exercise has a positive effect on mechanical and morphological characteristics of tendon tissue[4,9]; most of the research, however, was done on animals and usually involved immature animals[9]. Exact loads applied were also not usually measured during these experiments[9]. Exercise appears to cause tendon remodelling with a transient period of mechanical weakness, during which period renewed exercise loading would seem to be contra-indicated[9]. An optimum range for volume, frequency, density, and loads used with exercise for rehabilitation and prevention of tendon injuries is unknown. It seems sound clinical practice to start tensile-loading programs very conservatively and to adjust exercise program variables to patient response.

Summary

- Evaluation of the patient with a tendon injury should

Table 2. Terminology of Tendon Injury (from Leadbetter WB. Cell-matrix response in tendon injury. Clin Sports Med 1992;11:533-578).

New	Old	Definition	Histologic Findings	Clinical Signs and Symptoms
Paratenonitis	Tenosynovitis Tenovaginitis Peritendinitis	An inflammation of only the paratenon, either lined by synovium or not	Inflammatory cells in paratenon or peritendinous areolar tissue	Cardinal inflammatory signs: swelling, pain, crepitation, local tenderness, warmth, dysfunction
Paratenonitis with tendinosis	Tendinitis	Paratenon inflammation associated with intratendinosis degeneration	Same as I, with loss of tendon collagen fiber disorientation, scattered vascular ingrowth but no prominent intratendinous inflammation	Same as I, with often palpable tendon nodule, swelling, and inflammatory signs
Tendinosis	Tendinitis	Intratendinous degeneration due to atrophy (aging, microtrauma, vascular compromise, etc.)	Noninflammatory intratendinous collagen degeneration with fiber disorientation, hypocellularity, scattered vascular ingrowth, occasional local necrosis or calcification	Often palpable tendon nodule that can be *asymptomatic*, but may also be point tender. Swelling of tendon sheath is absent
Tendinitis	Tendon strain or tear A. Acute (less than 2 weeks) B. Subacute (4–6 weeks) C. Chronic (over 6 weeks)	Symptomatic degeneration of the tendon with vascular disruption and inflammatory repair response	Three recognized subgroups: each displays variable histology from purely inflammation with acute hemorrhage and tear, to inflammation superimposed upon pre-existing degeneration, to calcification and tendinosis changes in chronic conditions. In chronic stage there may be: 1. Interstitial microinjury 2. Central tendon necrosis 3. Frank partial rupture 4. Acute complete rupture	Symptoms are inflammatory and proportional to vascular disruption, hematoma, or atrophy-related cell necrosis. Symptom duration defines each subgroup:

Data from Clancy WG: Tendon trauma and overuse injuries. *In* Leadbetter WB, Buckwalter JA, Gordon SL, (eds): Sports-Induced Inflammation. Park Ridge, IL, American Academy of Orthopaedic Surgeons, 1990; and Puddu G, Ippolito E, Postacchini P: A classification of Achilles tendon disease. Am J Sports Med 4:145–150, 1976.

include an ergonomic analysis of the work place or an analysis of technique and equipment used in sports, and a physical evaluation focused on contributing or causative impairments within the musculoskeletal system.

• Patient history should include the factors known to contribute to injury and enquire into the presence of repeated or prolonged symptoms of injury to tendon and peritenon leading to the suspicion of tendinosis.

• Assume that the injured tendon is in the vascular-inflammatory phase, unless proven otherwise.

• Instituting a progressive tensile loading program should start conservatively and adapt load, volume, frequency, and density to patient response.

Acknowledgement

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