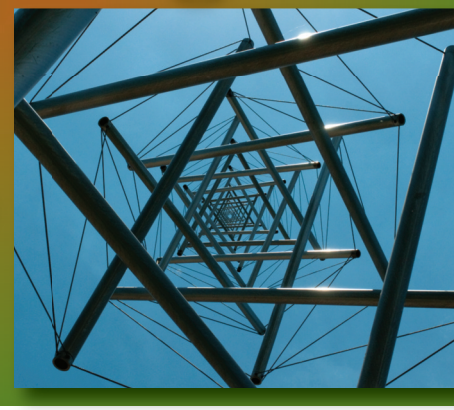
Continuing Medical Education

Overuse Injuries of Tendon and Bone: All the Small Things

Here's the current evolution in thought, literature, and treatment of these conditions.



Objectives

After completing this continuing education article, the reader should be able to:

1) Outline mechanotransduction and the new field of mechanobiology and their relationship to overuse bone and tendon injuries.

2) Describe cellular architecture as a feature of the cytoskeleton based on tensional relations between microtubules and microfilaments.

3) Delineate the physical, biochemical and genetic features of overuse injuries of tendon, including Achilles tendinopathy and rupture.

4) Describe the latest literature results for the therapy of Achilles tendinopathy including eccentric stretching, platelet rich plasma, and ESWT.

5) Describe the effects of cyclic loading on bone and tendon.

6) Describe differences between males and females in the causes and risks of overuse injuries.

7) Understand bone as a cellular and interconnected network of tissue and be able to describe how mechanical forces affect bone remodeling.

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*Following this article, an answer sheet and full set of instructions are provided (p. 172).—**Editor***

By Stephen Pribut, DPM

Introduction

Exercise is good for what ails you. It can improve memory, lower the risk of chronic disease, lessen the risk of diabetes, heart disease, stroke, and contribute to maintaining a healthy body weight. But, when done to excess, running can be the cause of overuse injuries and run you into the ground. Overuse injuries occur frequently among runners, causing downtime, and having deleterious physical and emotional consequences. This article will examine the features and describe the diagnosis and treatment of tendon and bone overuse injuries. Recent theories on cell and tissue mechanics will be discussed in the context of overuse injury.

Mechano-biology: Let's Get Physical

When a patient presents with an overuse injury, we often think of the clinical aspects of the problem. We may try to analyze the events that

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led up to the injury and how to improve the condition to enable the patient to return to the sport. In doing so, we select to read on overuse injuries, but we often forget about what is going on at the cellular level. The genome has been one of the main foci of discussions of performance and disease, but we should also look at a newly developing discipline: mechano-biology.[1-3] Biochemistry, biophysics, physiology, anatomy, biomechanics, and cellular mechanics all come into play in this field, with significance for a variety of clinical entities including overuse injuries. We think of the diabetic with a chronic ulceration and the distance runner as vastly different. However, many of the tissue structures and components important in wound healing are also critical to the healing of overuse injuries.

For all the elegance of genomics and biochemistry, mechanics still plays a major role in health and disease.[4,5] The mechanical loading that occurs with each step and with each movement that a joint undergoes is critical to maintain healthy articular cartilage. Intermittent contractions of muscles and the mechanical forces of loading thereby applied to muscles, tendons and bone result in remodeling and reshaping of these tissues.

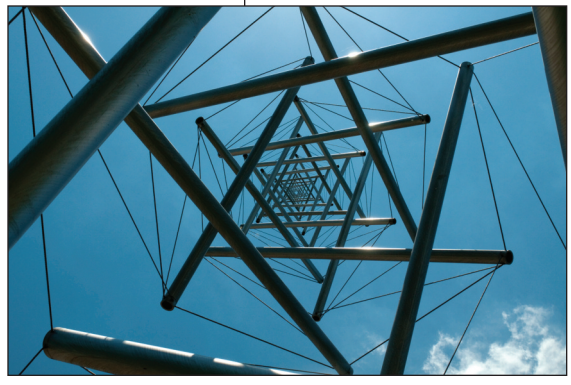

Figure 1: The Needle—Kenneth Snelson's Tensegrity Sculpture (Washington, DC outside of the Hirshorn Museum)

Julius Wolff, a nineteenth century anatomist, proposed in 1892 that bone remodeled according to the stresses placed upon it.[6] This has since become known as "Wolff's Law". From this simple and clear observation, we have progressed to the more general concept of mechano-transduction.

Cellular Mechanics and Mechanotransduction

It has become apparent that mechanical forces play a major role in the regulation of cellular activity.[7,8] The role is becoming increasingly clear for mechanical forces in biological and genetic activation, cellular proliferation, tissue morphogenesis, and even in the growth of malignant tissue.[2,4,9-11] Mechano-transduction is the method by which optimal mechanical stress acting on a cell is detected, thereby stimulating intracellular signaling, promoting cellular activity including cellular growth, and enhancing cell survival. The forces acting on the cell through mechano-transduction affects cellular morphology and architecture and has an impact on the metabolism and genetic expression of the cell. It is important to realize that mechanical forces can strengthen and enhance repair of the connective tissue, as well as acknowledge that aberrant forces can also stimulate the breakdown of that tissue. Mechano-transduction is just starting to be recognized as possibly being central to much of physical therapy and massage therapy. It is likely one of the reasons why early mobilization following injury is helpful and may also contribute to the benefits of other mechanical therapies including taping, bracing, and custom orthotics.[12]

Buckminster Fuller and the Architecture of the Cell

Donald Ingber used the term "tensegrity" to refer to the tensile integrity that cells exhibit as a result of their cytoskeleton.[13] The term was coined by Buckminster Fuller to describe structures made by the sculptor Kenneth Snelson in 1948.[14] Fuller designed many of his own structures along similar principles (Figure 1).

A tensegrity structure is self-supporting and includes a set of rigid elements such as struts, with endpoints that are connected to each other by continuous tensile connectors such as strings. The internal balance and self-created tensions create equilibrium by virtue of the compression of struts and tension of strings which allow the structure to maintain its shape. Geodesic domes and self-supporting camping tents are examples of tensegrity structures (Figure 2).

Figure 2: Another view of The Needle

The old concept of a cell as an amorphous blob of protoplasm surrounded by a gelatinous membrane is definitely out. This image of the cell does not allow for force transmission within the cell. Instead, a specific "solid" cytoskeleton provides structure to the cell.[15] The cytoskeleton is made of three filament systems: microfilaments, intermediate filaments, and microtubules. Microfilaments are made of actin that associates with myosin to make tension-generating 'contractile filaments'. Actin by itself can form a flexible network or self-assemble into rigid cross-linked bundles. Intermediate filament composition varies according to cell type. These cells are polymers made from a variety of proteins including keratin, desmin, or vimentin. They form "flexible cables" extending from the cell surface to the cell center surrounding the nucleus.

The cellular architecture is essentially a network of what Ingber terms "molecular cables, ropes, and struts that span from the nucleus to the surface membrane". Ingber believes that the cell is no Jello-like blob, but rather its tensional integrity provides for shape stability or "tensegrity." Tensional forces develop within the cell as the actomyosin filaments slide within the cell. These forces are transmitted and balanced both with-

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in the cell, and may be transmitted to other cells via external adhesions to the extra-cellular matrix (ECM).

Mechanically, the cytoskeleton acts as a system of struts and strings to internally balance forces. The cell transforms mechanical forces into biochemical signals and actions. Ingber's view has come to be widely accepted, and mechanobiology has become a growing discipline. Ingber further demonstrated that integrins are the receptors transmitting signals that result in changes to cell shape which regulates gene expression and DNA synthesis. Integrins are transmembranous protein chains that are integrated into the cellular membrane, extending from the extracellular space across the membrane into the intracellular space.

ECM and Mechanics as a Determinant of Cellular Control

The extra-cellular matrix (ECM) is a mix of a variety of materials. In a sense, it creates a flexible network that essentially transforms mechanical loading into intracellular signals. Proteoglycan molecules (PG), integrins, and dystroglycan all combine to form a scaffold for the adhesion of cells. The forces transmitted through this network both activate cellular signaling pathways and initiate cellular cytoskeletal rearrangement. Growth factors contained within the ECM are released following mechanical stimulation. Integrins are thought to be the main sensors of tensile stress at the cell surface. Extracellular matrix sites which interact with integrins include collagens, fibronectin, tenascin, and laminin.

The biological processes which affect cell growth, differentiation, polarity, motility contractility, and apoptosis are all subject to the influence of mechanical forces acting on cells that alter their physical shape. Fibroblasts, chondrocytes and capillary endothelium can have their activity changed from growth to differentiation by a decrease in the stiffness or in the adhesivity (Ingber 2003). Diseases of Mechano-transduction}. Endothelial cells can be converted to increase their rate of apoptosis. Individual bone cells have been shown to produce new bone in response to mechanical stress in vitro, just as they do in aggregate in vivo. Tensional forces have been observed to promote capillary outgrowth in vitro. The studies performed have demonstrated the importance of physical force in altering cellular activities and behavior without reliance upon hormonal or cytokine influence.

TABLE 1a

Selected Mechanical Therapies

- Acupuncture
- Anti-arrhythmic drugs
- Bone fracture healing
- Botox
- Distraction osteogenesis
- Massage therapy
- Orthotics—custom
- Physical therapy
- Vasodilator therapy
- Vacuum assisted wound closure

TABLE 1b

Selected Diseases with Possible Mechanical Etiology

Selected Disorders Associated with Possible Defects of Mechanotransduction

- Neurotrophic Ulceration
- Arteriosclerosis
- Hyperkeratoses
- Deafness
- Adult Respiratory Distress Syndrome
- Hypertension
- Sickle Cell Anemia
- Tendinopathy
- Osteoporosis
- Stress fractures
- Plantar fasciitis
- Posterior tibial tendon dysfunction
- Hypertrophic cardiomyopathy

Tendons

Tendons transmit the contractile forces of muscle to bone, effecting movements. The shape, size, and angle of application of the tendon affect the forces generated. Tendons are designed to withstand large loads during locomotion. While running, the Achilles tendon can come under a load of up to eight times one's body weight. A tendon's ability to stretch, and the intramuscular connective tissue's ability to store and release elastic energy serve to increase the efficiency of locomotion. Normal tendon tissue is white, firm and has a fibroelastic texture. Tendon has a tensile strength of 5.0 kN/cm2 to 10kN/cm2, higher than that of bone.

Tendons, like the other parts of the musculoskeletal system, need to be used and placed under a certain amount of stress to obtain optimum health. However, bouts of repetitive loading without adequate recovery time or at abnormally high loads can result in overuse injuries such as tendinopathy. Tendinopathy is a common problem in runners and can be resistant to therapy. The mechanism of injury is still being researched, but today's conceptualization of tendon function and injury is quite different than that of 20 years ago. While tendons have been thought to be relatively inert, mechanical loading induces considerable metabolic changes.

Tendon is made of dense connective tissue consisting predominantly of collagen. The collagen molecule is 1.5 nm in diameter, and approximately 300 nm long. In order of ascending structural complexity, collagen is a triple helix (type I collagen consists of two identical alpha strands and one beta strand) called tropo-collagen which is organized into fibrils and makes up the fibers or primary bundles of tendon. The fibers are grouped into fascicles (secondary bundles) and tertiary bundles which ultimately are organized into the entity we call a tendon. The basic unit of the fibril allows for limited damage to occur, which prevents the tearing of one small portion from spreading throughout the structure. Tendon is 55-75% water, with much of this water associated with proteoglycans

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in the ECM. The tendon dry weight contains 60-85% collagen. Type I Collagen predominates at about 60% or more of the dry mass of tendon, while elastin constitutes only about 2%. There are about 28 types of collagen proteins, but only a few are important components of tendon.

Tenocytes and tenoblasts (spindle shaped, immature tendon cells) make up 90—95% of the cells of tendons. The tenoblasts transform into the less metabolically active tenocytes as they age. The remaining cellular components of tendons include chondrocytes at the insertion point, synovial sheath cells, and vascular cells of tendon blood supply. Tenocytes manufacture all of the components of the ECM, produce collagen, and participate in metabolic energy production. As the cells age, the metabolic processes change to more anaerobic production of energy.

Tendinopathy is the clinical term for unhealthy tendon resulting from overuse injury. Tendinosis and tendinitis are specific histo-pathological diagnoses. Overuse tendinopathies result in pain and loss of strength, motion, and function. Tendinopathic tendon exhibits little to no inflammation. There is an increase in cellularity, an increase in proteoglycan content, increased vascularization, and a loss of the tightly bundled collagen appearance. The tendinopathic tissue is usually grey or brown and is soft and fragile.

Go with the Force

Tendon is usually viewed as a simple, unitary structure that transmits force. The reality may be more complicated. There is evidence that suggests that force is not transmitted evenly throughout the tendon. Stresses and strains may be distributed differently in deeper portions of the tendon in comparison with superficial sections. Studies in human patellar tendon have demonstrated different mechanical properties of the anterior and posterior portions of the tendon. (Haraldsson. Region specific mechanical properties of the human patella tendon. *J Appl Physio* 2006) This suggests that forces applied to a tendon would not be evenly distributed throughout a cross-section of the tendon. It is possible that shear forces within the inter-fascicular spaces serve to stimulate collagen production in the fibroblasts.

While knowledge is rapidly increasing in the science of tendinopathy, we still know little about even the length of the collagen fibrils within a tendon. There is contradictory evidence on whether or not fibrils are continuous or discontinuous. If the tendon fibrils are continuous, the local tension would be borne by an individual fibril. If the fibrils are discontinuous, the forces would be transferred to the adjacent fibrils and shearing forces would be of greater significance. This leads directly to another question: Is the injury a micro-rupture of a tendon fibril or are the components of the ECM playing a major role in injury and being damaged by shear forces?

The movement, stretching, and dissipation of local strains could take place in either, or a combination, of three possible mechanisms (Magnusson 2010):

1) The triple helix of the tropocollagen may elongate.

2) The gap between longitudinally oriented fibers may increase.

3) A relative slippage may occur between adjacent molecules.

Repetitive tensile loading mechanically alters the shape of the fibroblast cells in tendons. This plays a major role in the mechano-transduction of physical force into genetic and biochemical action. Over-loading may result in injury or a material fatigue of the tendon tissue. Too little stress will also have a major impact on cellular function. Somewhere between the extremes of too little or too much strain, the tissue will reach a proper balance of synthesis and degradation of tissue.

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TABLE 2
Histology of Tendinopathy

Decrease in numbers and a rounding of fibroblast cells.
An increase in proteoglycans, glycosaminoglycans, and water.
Increased vascularity.
Disorganized collagen fibrils.
Tendinopathic tissue may also demonstrate an increase in substance-P positive nerve fibers and androgenic receptors.
An increase in the number of apoptotic cells is seen.
No inflammatory cells are seen.

TABLE 3
Altered Levels of mRNA Comparing Tendinopathic Tendon with Rupture
(data extracted from Jones et. al., 2006)

	Tendinopathy	Ruptured Tendon
Higher Gene Expression		
MMP	-11, -16, -23	-1,-9,-11,-14,17,19, 25
ADAMTS	-2,-3	-4
ADAM	-12	-8, -12
TIMP	-	-1
Lower Gene Expression		
MMP	-3, -10, -12, -27	-3,-7,-24, 28
ADAMTS	-5	-7, -13
ADAM	-	-
TIMP	-3	-2,-3,-4

Tendon...

Characteristics of Tendinopathy

Histology

Tendinopathic tissue demonstrates a variety of alterations to cellular structure, cellular function, and to the ECM. The fibroblasts (tenocytes) are reduced in number and more rounded. The ECM shows an increase in proteoglycans, glycosaminoglycans, and water. Collagen fibers are disorganized. Substance-P nerve fibers and adrenergic receptors are found. Apoptosis occurs to a significantly greater extent in tendinopathic tissue. Inflammatory cells are not seen. These changes are outlined in Table 2.

Myth Busting: Does Tendinopathy Precede Rupture?

While some feel that Achilles tendon ruptures are preceded by tendinopathic changes, we don't know what accounts for chronic Achilles tendon pain which continues for years without ever progressing to a rupture. Recent research and careful analysis of the data have led other investigators to note that there are subtle but critically important differences in the biogenetic profile of individuals who suffer from tendinopathy compared with those who have suffered a rupture of the Achilles tendon.[16,17] If we view all collagenases, MMPs (matrix metalloproteinases), TIMPs (tissue inhibitor of metalloproteinase) and ADAM (a disintegrin and metalloproteinase) proteins as being alike, we will make as large an error as if we perceived all lipoproteins such as HDL and LDL as having the same function.

Jones, et al. examined the genetic expression of the Achilles tendon in normal, tendinopathic, and ruptured patients. The authors noted that "As many differences were observed between the chronically painful and ruptured tendons as were observed between either of the pathologic tendon groups and the normal tissue group".[16] In a recent review article, Magnusson, Landberg, and Kjaer state that "the molecular 'blueprint' of tendinopathy is quite different from that of tendon rupture".[17]

The structural characteristics of the tendon arise in large part out of the properties of the extracellular matrix (ECM). The ongoing balance of synthesis and degradation is impacted to a large extent by the proteinases (such as collagenase), which have several regulatory points including transcription, translation, or via interaction with interconnectors. The ECM is in a state of dynamic anabolic/catabolic equilibrium. The matrix metalloproteinases (MMP) are a family of more than 20 zinc-dependent endopeptidases which can degrade most of the constituent parts of the ECM. They play vital roles in both health and disease states. The MMP category of enzymes includes collagenase I, collagenase II, and collagenase III. The tissue inhibitors of metalloproteinases (TIMPs) are physiological inhibitors of the MMPs. TIMP group proteins also mildly inhibit the ADAM and ADAMTS group of proteins. The balance of all of these proteins is important in the regulation of healthy tissue. Pasternak and Aspenberg recently published an excellent review of metalloproteinases and their inhibitors.[18]

Jones, et al. examined the mRNA expression of enzymes involved in extracellular proteolysis in normal, tendinopathic, and ruptured Achilles tendon.[16] Contributors to this system of enzymes include the matrix metalloproteinase (MMP), (ADAM), and ADAMTS groups. Of 50 gene groups of enzymes investigated, 33 were found to be different among the three tendon conditions. Both the painful and ruptured groups have a lower level of MMP-3 and TIMP-3. They both exhibited a higher level of ADAM-12 and MMP-11 mRNA.

Table 3 (with data from Jones, et al., 2006) details the differences between the tendinopathic and ruptured groups.

The authors concluded that the mRNA expression over the genome was different for each tendon group, and indicated that each group represented a unique biological state. Elevated levels of messenger RNA (mRNA) were found for type I and III collagens, proteoglycans (such as biglycan and fibromodulin), angiogenic factors including vascular endothelial growth factor (VEGF)), aggrecan, heat shock protein (HsP), fibronectin and tenascin C, and proteolytic enzymes (such as a disintegrin and metalloproteinase or TIMP). These proteolytic enzymes are both important to healthy tendon, but in abnormal amounts will lead to pathological changes.

In spite of the upregulation of mRNA for type I collagen, there was no increase in type I collagen protein. Type III collagen increases in tendinopathic tissue. This is another indicator that the normal homeostatic mechanisms are not functioning. The specific findings included a number of differences in mRNA expression. There was a lower level of MMP-3 and TIMP-3, along with a higher level of ADAM-12 and MMP-11 mRNA found in both of the pathological tendon groups (both painful and ruptured) compared to the normal tendon group.

In the painful tendon group compared to the normal tendon group there was a lower level of ADAMTS-5 and MMPs 10, 12, and 27, along with a higher level of ADAMTS-2 and -3 and MMPs 16 and 23 mRNA.

The ruptured tendon group compared to the normal group showed a lower level of ADAMTS-7, MMPs 7, 24, and 28, and TIMPs 2 and 4, with a higher level of ADAM-8, ADAMTS-4, MMPs 1, 9, 14, 19, and 25, and TIMP-1 mRNA.

The ruptured group compared to the painful tendon group demonstrated a lower level of ADAMTS-2, -3, and -17, MMPs 7, 16, 23, 24, and 28, and TIMPs 2, 3, and 4, along with a higher level of ADAMs 8 and 12, ADAMTS-4, MMPs 1, 8, 10, 12, 19, and 25, and TIMP-1 mRNA.

There were as many differences between the chronically painful and ruptured tendon groups as were seen between either the ruptured group or the painful group in comparison with the normal tissue group.[16] In their discussion, Magnusson et al. (2010) briefly mention an "intervention model that combines immobilization with acute loading" as a possible future area of research to improve our understanding.[17] A modification of that

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approach employing pneumatic walking boots with graded exercise may be helpful in the treatment of resistant Achilles tendinopathy.

The MMP/TIMP systems which play such an important role in the dynamic balance of production and degradation of tissue may be a suitable candidate for future research and intervention. The currently known MMP inhibitors, such as tetracycline derivatives, have not yet been found to be helpful in treating overuse injuries.[18] Bisphosphonates, which inhibit osteoclastic bone resorption, also inhibit MMPs.

Cyclic Loading and the Healthy Tendon

Normal tendon activity increases collagen synthesis, while inactivity lowers both the collagen synthesis and collagen turnover. Some amount of activity is necessary to spur normal collagen formation, even in tendinopathic tissue. A question that is hard to answer is how much of a role should eccentric exercises play in the therapy of severely damaged tendon.

Mechanical loading causes an increase in mRNA linked to collagen expression and increased synthesis of collagen. IGF-1, transforming growth factor -beta (TGF -beta), connective tissue growth factor (CCTGF), and interleukin 6 (IL-6) all increase in response to exercise. Strain loads lead to a two to three times increase in collagen formation which peaks 24 hours after exercise and remains elevated for up to 70 or more hours. Degradation of collagen proteins also increases after exercise and starts even sooner than the collagen formation. Proteolytic markers, MMPs and collagen degradation fragments are elevated after exercise for 18 to 36 hours. These changes decrease after adaptation to exercise. Unaccustomed exercise stresses the tissues more than accustomed exercise and has a greater impact on the balance of anabolism and catabolism. Insufficient recovery time (or the "too little rest" of the "terrible too's") is another likely key to tendinopathy.

Angiogenesis

Formation of new blood vessels is a feature of healing tissue and injured tendons. Angiogenesis is also a factor in cancer, diabetic retinopathy, and macular degeneration. Vascular endothelial growth factor (VEGF) antagonists have recently been approved to treat macular degeneration, and someday may be useful for tendinopathy. Angiogenesis is a factor in both tendinopathy and its recovery. Oncology research into vascular growth factors is also relevant to tissue-healing and to cellular mechanics. A recent article detailed both in vitro and in vivo factors and showed that the mechanical features and stiffness of the ECM had a substantial impact on angiogenesis via VEGFR2.[19] This study demonstrated the first known functional cross-antagonism between transcription factors of tissue morphogenesis. The antagonistic transcription factors TFII-I and GATA2 control the genetic expression of the VEGF receptor VEGFR2. This thorough study showed that the VEGF system responded to both mechanical and chemical factors.

Genetic Screening for Risk of Tendinopathy

There has long been a suspicion that both tendon repair and tendinopathy are affected by genotype. While the risks are multifactoral, specific genetic associations are being delineated. The genes responsible for collagen production are likely candidates to examine. Type I Collagen is the primary structural constituent of tendon and ligaments. It is a heterotrimer consisting of two alpha-1 and one alpha-2 chains. The COL1A1 (collagen type I, alpha-1) gene sometimes has a single nucleotide polymorphism (SNP) rs1800012 in its first intron in which a G (guanine) to T substitution occurs (known as the TT genotype), which has been associated with protection from soft tissue injuries such as Achilles tendon rupture and ACL ruptures.[20] This 'TT genotype' is also under-represented in cases of Achilles tendinopathy.[21]

Research, this year, has investigated alleles of the TGF-beta (tissue growth factor), previously thought to possibly enhance tendon repair) and an allele of the growth/differentiation factor-5 (GDF-5). The allele GDF-5 TT genotype of GDF-5 rs143383 variant was found to be associated with twice the risk of developing Achilles tendinopathy, while occurrence of the TGF-beta 1 allele was not found to be significantly different in the control and tendinopathic populations.[22]

Achilles Tendinopathy Update

The Achilles tendon is one of the best studied and most often injured tendons. The Achilles tendon connects the most powerful muscle in the body with the calcaneus. This tendon is named after the legendary Greek hero Achilles, who according to myth, was protected from wounds by being dipped in a magical pond by his mother, Thetis. She held him by the heel, which was not immersed. He died during the Trojan wars when Paris launched a poisoned arrow that struck Achilles in his heel as described in Homer's *Illiad* (700 BC). Although injuries to this area have been known for more than 2,000 years, it was first reported in the medical literature by Ambroise Paré only 400 years ago.[23]

Anatomy

The Achilles tendon joins three muscles: the two heads of the gastrocnemius and the soleus. The heads of the gastrocnemius arise from the posterior portions of the femoral condyles. The soleus arises from the posterior aspect of the tibia and fibula.

The gastrocnemius is a multijoint muscle crossing three joints: the knee, the ankle, and the subtalar joint. The soleus does not cross the knee and is a biarticular muscle. The plantaris is a nearby muscle that has its separate tendon that arises from the lateral condyle of the femur. It has a thin tendon that passes between the gastrocnemius and soleus and inserts into the calcaneus. When this musculotendinous structure is injured, it is frequently felt as a "pellet shot" in the back of the leg. The tear is usually about eight inches below the knee joint. Plantaris injuries, once controversial, have been documented surgically and on MRI.[24]

The bulk of the Achilles tendon inserts into the posterior superior third of the calcaneus. Some fibers

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course distally and continue to where portions of the plantar fascia insert into the plantar aspect of the calcaneus. There is a continuity of the insertion with the most distal aspect of the insertion being contiguous with the plantar fascia.

The Achilles tendon does not have a rich blood supply. The blood supply has been found to be weakest at a point between 2 and 6 cm above its insertion into the calcaneus. It is not invested within a true tendon sheath. A paratenon composed of other soft tissue surrounds it. The outer layer is a portion of the deep fascia, the middle layer is called the mesotenon and the inner layer is contiguous with a thin layer surrounding the tendon itself (epitenon). The blood supply to the proximal portion of the tendon comes from the branches of the muscles themselves. The distal portion is supplied by branches from the tendon-bone interface. The mesotenon supplies the major blood supply to the Achilles tendon.

Findings

Symptoms of Achilles tendinopathy include thickening and visible swelling of the tendon, pain on hopping, pain while running, and tenderness upon palpation. Often morning stiffness is found.

Tendinopathy may refer to tendinitis, paratendinitis, and later stage chronic tendinosis. Histological studies have demonstrated that those with chronic tendon pain do not have inflammatory changes, but instead show degenerative changes in the affected tendon.[25] Tendinosis refers specifically to tendons with known chronic degenerative changes. The term tendinopathy itself does not have this connotation as applied to overuse tendon pain and swelling in the absence of a histopathological diagnosis. In long-standing tendinopathy, the tissue exhibits mucoid degeneration. The tissue is brown or yellow, is disorganized, and has a lack of defined tightly bundled collagen fibers. Microscopic examination reveals degenerative changes and concomitant fibrosis.[26] Ultrasound examination reveals neovascularization in the injured tissue.

Achilles tendon disorders are often divided into three zones: 1) Non-insertional—the tendon proper (and paratenon), 2) conditions affecting the tendon insertion, and 3) proximal—at the muscle tendon interface and more structures proximal.[27,28] An outline and table describing the classification is available in a previous article published in *Podiatry Management*.[29]

Insertional Enthesopathy

Tendinopathy may occur at the insertion of the Achilles tendon or within the main body of the tendon itself. It is possible that these two differing areas may result from diverse predisposing factors. It has been suggested that repeated stresses that are well within a clinical and functional range may create the pathology in a manner similar to the way in which bone stress reactions may occur.[30] The major contributing causes cited include overuse, abnormal biomechanical factors, fluoroquinolone antibiotics, and corticosteroid use.

A study published in the Journal of the American Medical Association earlier this year found PRP to work no better than saline for the treatment of Achilles tendinopathy.

At the insertion of the Achilles tendon, a variety of conditions may occur. In addition to insertional tendinopathy of the Achilles tendon, one may find retrocalcaneal bursitis, Haglund's deformity, and pre-tendinous bursitis. When the Haglund's deformity is symptomatic, it is usually found as a triad of insertional tendinopathy of the Achilles tendon, a prominent postero-superior calcaneal process, and retrocalcaneal bursitis. Insertional tendinopathy can occur in the absence or presence of calcaneal bursitis. Numerous studies indicate that insertional tendinopathy occurs in up to 5%—20% of Achilles tendon overuse injuries.[31] Older individuals appear to be at higher risk for this injury.[31]

The insertion of the Achilles tendon consists of tendon, fibrocartilage and bone. Three types of cartilage are found here: sesamoid, periosteal, and enthesial fibrocartilage. What has been termed an insertional tendinopathy might more correctly be called an insertional enthesopathy. The fibrocartilage functions to resist shear and strains at the enthesis. Bone spurs at this location do not form within the substance of the tendon itself. Clinically, pain and tenderness are present at the back of the heel. The pain is aggravated by running uphill, and by prolonged walking, standing or running.

Non-Insertional Achilles Tendinopathy

The Achilles tendon is most often affected in noninsertional tendinopathy at a location 2 to 6 cm proximal to its insertion into the calcaneus. The paratenon substitutes for a true gliding synovial sheath. It is comprised of fatty areolar tissue surrounding the Achilles tendon and is organized into a mesotenon. Werd has pointed out how to distinguish tendinopathy from paratendinopathy.[27] Palpate the painful area while the foot is dorsiflexed and plantarflexed. If the area of maximal tenderness does not move, the presumption is that the site of tenderness is within the paratenon itself, which is firmly attached to the surrounding tissues and does not move. If the tenderness shifts with dorsiflexion and plantarflexion, the tenderness is deemed to be within the tendinous tissue.

Sex and the Tendon

Women appear to have a higher incidence of certain connective tissue injuries. Stress fractures and anterior cruciate ligaments (ACL) are among those often cited. A study of military cadets in training demonstrated a 2.5 times higher incidence of injury and a 3.9 times higher in-

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cidence of hospitalization among the female cadets.[32] The authors suggested that improved pre-training and a more gradual adaptation were needed to lessen injuries. A close examination of the data revealed that the injury rate seemed to be inversely correlated with running speed. The slowest female runners (lowest quartile) were three times more likely to have an injury. Those who were in the top quartile had a similar injury rate to the men of similar speed.

Tendons may be more susceptible to the influence of the changing levels of estrogen over the course of the menstrual cycle. Estrogen receptors are found on fibroblasts in tendon and ligament. Research on estradiol and other hormones has been done both in humans and animals, in vivo and in vitro. However, the studies do not provide a clear answer on the impact of estrogen on tendon health.[33] Some in vitro studies have shown a stimulating effect on fibroblast proliferation and collagen synthesis, while others have reported no effect, or even an inhibiting effect. More in vivo studies are needed to clarify the impact of estrogens on connective tissue.

Achilles and patellar tendon cross-sectional area (CSA) is greater in men than in women. The CSA is greater in trained men than in untrained men, but there is no significant difference in the CSA between untrained women and trained women.[34] This indicates a differential response to training in women in comparison to men. The authors concluded that the women's tendon had an attenuated response to training.

There is growing evidence that estrogen decreases the formation of large collagen fibers and overall synthesis of collagen. Hansen et al. compared contraceptive users (HE-OC) at a time of high estrogen and non-oral contraceptive users (LE-NOC) at a time of low blood estrogen and found a significantly greater increase in tendon collagen synthesis in the LE-NOC group following training.[35] They found no difference in the HE-OC group in tendon collagen synthesis 24 hours post-exercise. There did not seem to be any clinical risks to the tendon among either group. The authors concluded that their study results were consistent with the hypothesis that estradiol inhibits tendon collagen synthesis. Further studies by these authors are ongoing and provide similar results.[36]

Bryant et al. suggested that monophasic oral contraceptives (MOCP) may improve tendon function by limiting fluctuations over the menstrual cycle.[33] Their study didn't detect mechanical changes in tendon over the course of the menstrual cycle in non-contraceptive users, but did find changes in tendon mechanical characteristics between those using the contraceptive and those who did not. There was a decrease in tendon compliance in the MOCP users, which was thought to be caused by long-term exposure to lower levels of estrogen.

Eccentric Training: Not a Panacea

Alfredson proposed the use of eccentric stretching and strengthening, employing heavy loads, which when performed as described, causes pain and is meant to do so.[37,38] Similar approaches have been suggested for several other tendinopathies, including patellar tendinopathy. Review articles examining eccentric strengthening as treatment for a number of tendons found the evidence weak and under-powered.[39] The current literature was described as having a "dearth of high quality research in support of the clinical effectiveness of EE (eccentric exercise) over other treatments in the management of tendinopathies."[39] Kingma et al. agreed that, while the technique appeared promising, "large methodologically sound studies ….are warranted."[40]

A recent study showed that women suffering Achilles tendinopathy do not benefit to the same extent that men do after 12 weeks of eccentric training.[41] This study compared women and men treated with eccentric training without the use of a concentric control group. Thirty one females were compared to forty four males with an average age of 50 and BMI of 26. The males noted a reduction in pain of 44%, while the females found a pain reduction of 20%. Neither of these numbers appears to be as good as one would like. The study also had a substantial drop out rate at 20%. Those who dropped from the study reported overwhelming pain 25% of the time, had surgery 16% of the time, and could not be traced 25% of the time.

Nørregaard et al. noted that few authors had duplicated the success of eccentric training seen in Alfredson's studies.[42,37] They compared eccentric training with routine stretching of the gastrocnemius and the soleus. Maximum improvement was seen at one year, and the two groups had equivalent results with no significant difference.

Studies with low numbers of subjects and high dropout rates do not bring us to the goal of using high level, high grade studies to formulate an evidence-based practice of sports medicine. Other fields note that studies of 200 to 300 have a low number of subjects, but somehow many journals look at studies containing fewer than 100 subjects and often as few as 20-30 as constituting a worthwhile study. As we look to move towards an evidence-based practice of sports medicine, we should insist on more rigorous studies with a larger number of subjects.

Treatment

Tendinopathy is primarily treated by conservative means. Movement plays a role in active recovery. Treatment is often directed to decreasing strain forces on the tendon and allowing the tissue to repair itself. Relative rest, absolute rest, or the use of a pneumatic walking boot may be required. A pneumatic walking boot permits weight-bearing while limiting strain forces in the tendon, and allows removal for exercise. This therapy is useful in resistant cases and for patients who have an antalgic gait, experiencing pain with nearly every step. Alterations in cyclic loading can increase collagen production and diminish the production of anabolic MMPs.[43]

NSAIDs are often used, and offer a decrease in symptoms and a more normal gait and motion pattern through pain reduction, al-

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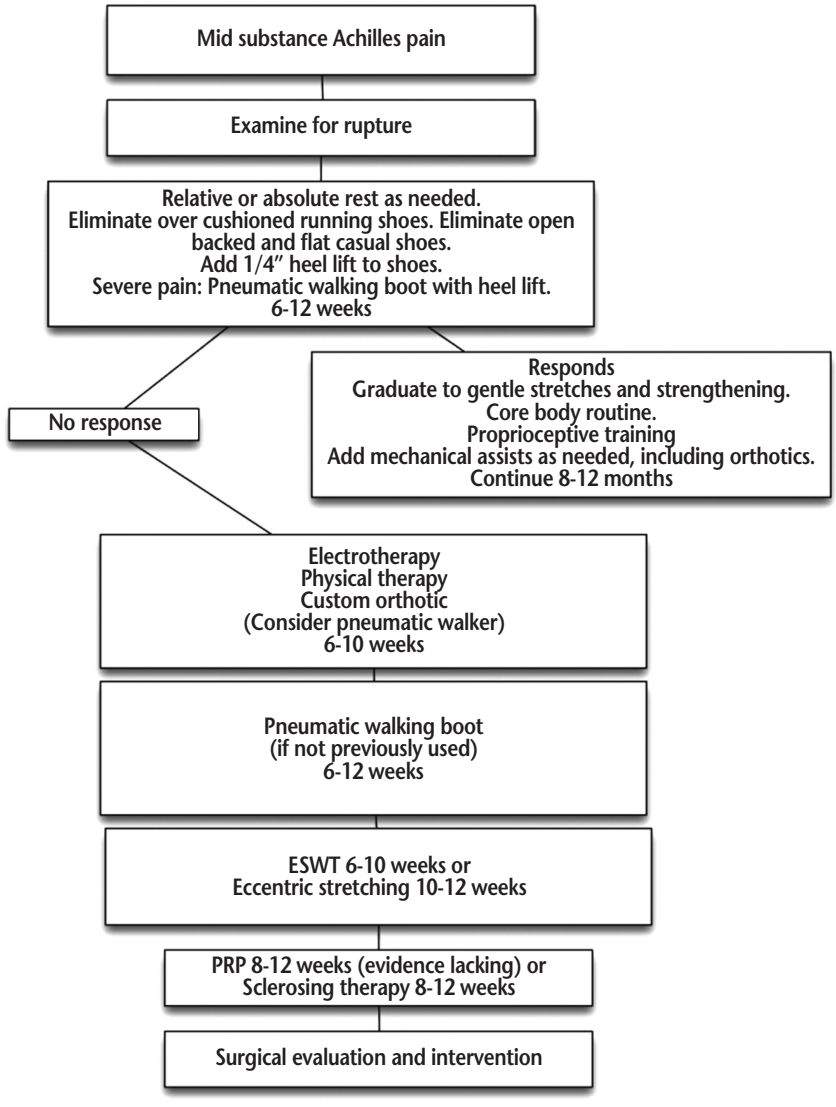
though their anti-inflammatory effects are no longer thought to be therapeutic.

Eccentric stretching is often mentioned as a cornerstone of treatment. However, while early studies of low numbers of patients by a limited number of groups were promising, other authors have trouble replicating the initial authors' results and find positive responses only in 50% to 60% of the patients.[44-46] Eccentric exercise has lost some of its luster among many clinicians.

Cross-friction massage and cryotherapy may be helpful. The modalities of ultrasound and high voltage galvanic stimulation may also be helpful. Heel lifts and custom functional foot orthotics may also assist in reducing mechanical strain. Heel lifts may significantly reduce strain forces within the Achilles tendon. Custom orthotics are often suggested and may decrease abnormal transverse plane tibial forces, believed to possibly be a contributing factor in Achilles tendinopathy.[47]

TABLE 4

Treatment Outline for Achilles Tendinopathy



After the pain is reduced, the patient may gradually return to activity. Hills and inclined treadmills should be avoided. Over-cushioned shoes, which increase the eccentric forces within the tendon, should not be worn. For severe, chronic and unremitting tendinosis, surgery remains an option. The described surgical procedures include stripping of the paratenon, linear tenotomies and excision of non-viable tissue.[31,48] There is little controlled data available on surgical procedures.

Platelet-rich plasma injection (PRP) has been said to have promise for soft tissue injury such as tendinopathy. So far, the literature has not backed up the promise. A study published in the *Journal of the American Medical Association* earlier this year found PRP to work no better than saline for the treatment of Achilles tendinopathy (Table 4).[45]

Bone Biology and Mechano-biology

Introduction

Bone is a dynamic and ever-changing tissue. It is part of an intricate system balanced in its resorption and production by mechanics and hormonal influences. While bone plays a structural role as a frame does to a building, it is a biological tissue that is capable of self-repair. Theories of bone development, functioning, modeling and remodeling have evolved. The mechanics of Wolff's law ultimately led to a time when the surface electrical changes, hormonal influences, and biochemical and genetic factors were thought to be most significant. A good deal of research has focused on these aspects of bone healing, but there has been a resurgence of interest in the importance of physical and mechanical influences.

The adaptability of bone is well known.[6] For many years, the understanding of boney adaptation has been on the functional adaptation of bone as a tissue. Cells, however, are what make tissue what it is. Although the general principle has been known for more than a century, the cellular mechanisms have not been well described.

From Wolff's simple and clear

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observation, our understanding of the "how" of bone modeling and remodeling moves on to the more general concept of mechano-transduction. Mechano-transduction is the manner in which mechanical energy is transposed into an electrical or biochemical biological signal. It is likely that most, if not all, eukaryotic cells are mechano-sensitive and respond to external forces. The physical world has many signals detected by our senses and cells. Gravity, sound waves, light waves, temperature, pressure, shear forces and impact shock are all in our environment, and change cellular functioning and ultimately structure. Adaptation to the physical environment has been the hallmark of life and its evolution. Signal detection and translation of these signals to biological information is the subject of study of mechano-biology.

Mechanical Stimulation at the Cellular Level

Osteocytes are thought to be the main mechano-sensory cells of bone, and the lacuno-canalicular network appears to be the mediator of the signals.[49] Strain-related flow of fluid through this system mechanically activates the osteocytes, and carries cell signaling molecules along with nutrients and waste products. Instead of gross-loading forces, lamellar fluid flow and the resultant shearing forces are likely the important signals received by bone cells, while induced local strain may be an additional signal. Jumping, vibration, and muscle contraction all create a variety of potential signals. Low magnitude but high frequency bone strains have been found to be anabolic to bone.[50] Disuse, aging, and sarcopenia all decrease direct loading of the bone and loading from muscle. This depresses the normal mechanical regulatory signal and results in bone loss. Exercise, vibration stimulation, and other protocols will ultimately be useful in prescriptions for recovery from bone injury.

Osteocytes are enclosed in lacunae surrounded by concentric lamellar layers of boney matrix. The osteocytes are connected to their neighbors by a network of interconnecting canaliculi. Both the osteocytes and the bone lining cells are remnants of the osteoblasts that have performed the productive work. Osteoclasts and osteoblasts are considered regulatory cells of modeling and remodeling. The osteocytes are strain-sensitive cells that translate mechanical signals derived from physical loads into biological activities. Osteocytes have dendritic processes that contact nearby cells at gap junctions and form a cellular network. The network extends from deep in the lacuna to the bone surface. Transduced signals are sent to both osteoblasts and osteoclasts. Proposed mechano-sensory sites include stretch-activated and voltage sensitive calcium channels (VSCC), focal adhesion proteins such as focal adhesion kinase (FAK), proline rich tyrosine kinase 2 (Pyk2) which are linked to the membrane by integrins, and G protein-coupled receptor (GPCR).

Bone has four surfaces which may undergo remodeling: the haversian system, trabecular, endosteal, and periosteal. Each surface differs in its response to remodeling signals. Appropriate mechanical stimulation received and mechano-transduced activates osteoblastic differentiation, proliferation, and apoptosis. Low levels of stimulation through inactivity or low gravity environment results in reduced bone synthesis and increased osteoclastic activity at the periosteal, endosteal, and trabecular surfaces. Aberrant forces also cause disruption of the normal balance of production and destruction of bone tissue. Pavalko, et al. describe a synthesis of how tensegrity theory could effect a mechanical and molecular cascade that would act directly on the nucleus.[51] Their pithy conclusion was that "bending bones ultimately bend genes".

The magnitude, duration, and frequency of the load modulate the response of the skeleton.[10] The mechanism underpinning mechano-detection and differentiation of signals resulting from axial loading, torsion, bending forces, and shearing forces remains to be worked out. Papachristou et al. (2009) recently summarized the currently hypothesized metabolic pathways triggered by mechanical stimuli.[52] Several contributing pathways have been mapped. Prostaglandin synthetase (PGES) and

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TABLE 5
A Quick Look at Stress Fractures

Virtually any of the bones of the lower extremity can suffer a stress reaction or stress fracture. Some of the most often injured bones include the tibia, metatarsal bones, navicular, femur, fibula, calcaneus, and cuboid. A few quick observations:

Metatarsals—most commonly affected foot bone for stress fractures. Injury most often occurs at the neck and shaft. If the injury has occurred at the base of the metatarsal, this may have been contributed to by vertical forces. Speed work, hill running, or running on the ball of the foot, are possible causes.

Cuneiform stress fractures—These injuries seem to occur from vertically oriented forces. Contributors to this injury include too much speedwork, hill running, or running on the ball of the foot.

Calcaneus—Clinical diagnostic test: squeeze the body of the calcaneus to elicit tenderness. Trace out the probable fracture line. If this area is not tender, and only the medial calcaneal tuberosity is tender, you more likely are dealing with an injury to the plantar fascia.

Tibia—Most frequently injured lower extremity bone.

Pelvic Stress fractures—May happen in running. Likewise the femur should be kept in mind as a potential site of stress reaction and stress fracture.

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COX 1/2 assist in the production of PGE2. COX-2 is also activated by PI3K/Akt and Wnt/ beta-Catenin. Mechanical loading activates the L-type voltage-sensitive calcium channel (L-VSCC), which allows the entrance of extracellular calcium to enter the cellular cytoplasm, inducing intracellular calcium release.

Mitogen-activated protein (MAP) kinases (MAPK) (serine and threonine kinases) are a major link between membrane receptors of environmental signals and altered gene expression. The MAPK cascade system ERK1/2 plays an integral role in upregulating COX-2. This correlates with research suggesting limiting NSAID use during early bone healing.[53]

The signaling systems implicated in mechanotransduction: Ca++ signaling, Wnt/ beta-catenin signaling, nitric oxide, prostaglandin signaling and integrin signaling pathways interact in a complex manner with the cells and the extracellular matrix (ECM). The genes controlling osteoblastic differentiation, proliferation, and survival respond by appropriate up-regulation and down-regulation.

Ultimately, delineating the mechano-responsive genes, molecular pathways, and signals which affect bone will have a major impact on therapy for bone-healing, injury prevention, aging, and osteoporosis.

Stress Injuries and Stress Reactions of Bone: Update 2010

Background

Chronic repetitive stress injury of bone, most commonly called a "stress fracture", has been described in the literature for many years. Cases have appeared in the literature going back to the 1800's. Briethaupt, a Prussian military physician, first reported this injury in 1855.[54] He presented the first description of a metatarsal stress fracture when he noted swelling and pain in the feet of military recruits. In 1897, just a few years after William Roentgen created the first x-ray machine, radiographic examination (x-ray) revealed the nature of these injuries. Injuries such as these were called "march fractures" because they commonly were seen in military recruits suddenly subject to long forced marches.[55]

Discussion and Definition

Stress-related bone injuries are frequent injuries among participants of running sports. In the absence of a visible fracture line, the bone is reacting to the stress, but it is not overtly cracked. X-rays may show periosteal bone formation, cortical thickening, or endosteal bone formation. Usually, there is a discrete area of boney tenderness. The out-of-favor term "stress fracture" implies a physical crack, which is how engineers think of stress or "fatigue" fractures. However, stress reaction or stress-related injury of bone better fit the overuse injury observed.

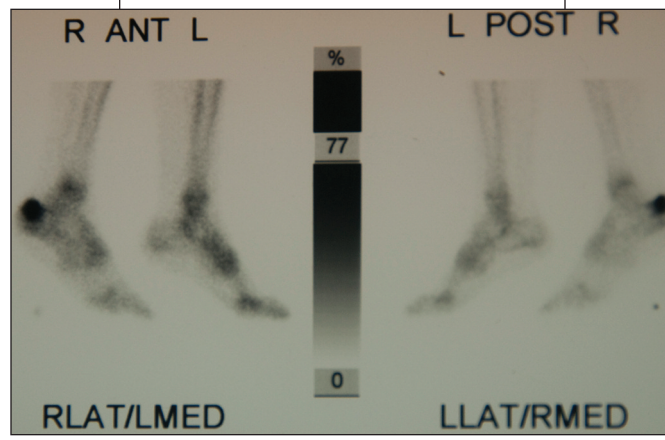

Figure 3: Calcaneal Stress Fracture

The initial injury might be a biological or biochemical abnormality or failure at the cellular or Bone Multicellular Unit (BMU) level. Bone adapts to many levels of intermittent, repetitive compressive and tension strains by an increase in density. However, in the presence of abnormally high and repetitive forces, the ability to heal from micro-damage is not adequate.[56] These excessive repetitive stresses occur without the bone having adequate rest to allow for adaptation to stress. The stress that creates these injuries is too much, too soon for the bone.

Runners most often injure the tibia, metatarsals, calcaneus, or cuboid. But all lower extremity bones may be affected including the femur, navicular, fibula, pelvis, and cuneiform bones. Excessive repetitive forces, which may be compressive, tensile, or complex, result in injury to the bone. The bone cells begin a process of resorption without significant bone production. The forces contributing to the injury are both directly transmitted, and also include forces generated by the "pull" of ligaments and tendons on the bone. Besides these external stressors to bone, the Haversian canals are subject to internal sheer forces created by fluid flow. The initial injury seems to be to the bone matrix itself and is hard to clinically measure or detect.

Note that the stress fracture in Figure 3 is anterior to the insertion of the Achilles tendon. This occurred after the patient began using a shoe which forced a forefoot landing, increasing the tension in the Achilles tendon. This demonstrates the devastating effect that tension can have on bone.

Injury may first be seen on a bone scan (scintigraphy) reflecting metabolic activity of bone. Slightly later, the injury will be visible on an MRI. Finally, the injury may become visible on an x-ray. Micro-fractures have been thought to be the physical precursor to stress-related injury of bone, but the reality is quite subtle. Mechanical forces activate the cell signaling mechanisms. Integrins, membrane proteins, thought to be a part of the cell-sensing system, appear to play a role in the activation. Aberrant forces alter the subtle balance between osteoclastic and osteoblastic activity through altered gene activity. This mechanotransduction of force into biological mechanism is the true precursor to the stress-related injury of bone. Cell-signaling alters the gene activation pattern which then changes the metabolic activity of the cells. The altered metabolic activity causes aberrant remodeling, which is a

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component of the initial stress "reaction" and not a true fracture (Table 5).

Contributing Factors

Training Errors

Training errors may be among the greatest contributors to this injury. A change in training such as increasing the frequency, intensity, or duration too quickly may contribute to injury. What has been termed the "terrible too's" of too much, too soon, too often, too fast, with too little rest cumulatively over-stress the bone before it can appropriately react to the stress by reinforcing itself.

Increased forces into the bones of the foot and leg are generated in the presence of fatigue. New marathoners may be subject to more fatigue than experienced runners if they rapidly build up their long runs. Fatigued muscles cannot properly position the bones, slow the forces, or attenuate the forces in any of several ways that normally-functioning muscles may do. Always emphasize to your patients to "...avoid doing too much too soon."

Equipment Errors

An improper match of foot type and shoe structure may contribute to a chronic repetitive stress injury to bone (stress fracture, stress reaction). Old, worn-out shoes are obvious contributors to injuries of all sorts. Running on a hard and unyielding surface may increase forces into the bones of the foot and leg. Concrete can be a significant contributor to this injury.

Systemic Disorders

A variety of systemic conditions can contribute to this injury. These conditions include osteopenia, osteoporosis, other metabolic bone disorders, hormonal abnormalities, inadequate nutritional intake, and collagen disorders. In women, amenorrhea or oligomenorrhea may lead to deficient estrogen and low bone mineral density. Women with amenorrhea may be up to five times as likely to develop a stress-related injury of bone.[57] The female athlete triad, by definition, includes low bone density, along with disordered eating (or low energy availability) and amenorrhea. Energy availability is dietary energy intake minus exercise energy expenditure. Low energy availability appears to be the primary cause of impaired reproductive and skeletal health in the triad.[58]

Overtraining may lead to decreased testosterone levels in men, resulting in osteopenia. Patients of either gender having multiple stress fractures should undergo a bone density (DEXA) scan.

Bone Geometry, Muscle Strength

Muscle cross-sectional area (MCSA) and bone geometry have been studied in relation to tibial stress fractures. A study of 39 female runners found that cortical bone strength, MCSA, and cortical area were all lower in those with stress fractures.[59] Popp et al. felt that greater muscle strength may prevent tibial stress fracture by decreasing the torque and shear forces going into the bone. Another study of 88 runners, male and female, found that tibial cortical cross-sectional area was inversely correlated with stress fracture and medial tibial stress syndrome.[60]

Immobilization in a pneumatic walker for four to six weeks or more is often helpful for tibial stress fractures, and a variety of other stress injuries of bone.

Edwards, et al. suggested that running speed was a risk factor for tibial stress fracture. A mathematical model was created and analyzed. The result suggested that by decreasing the speed of running from 4.5 to 3.5 meters/sec., the estimated risk of stress injury would decrease by 7%.[61] This is not a dramatic reduction, and real life data have indicated the opposite. Bijur, et al. studied 585 West Point cadets and found that injuries occurred less often in faster cadets.[32]

Diagnosis

Patients usually relate a sudden or sub-acute onset of pain. Questioning may reveal changes in exercise pattern or gear. Mileage may have recently increased, twice a day runs undertaken, aggressive speed work started, or the athlete may have worn his last pair of running shoes too long or changed to a very different new pair of running shoes. Physical examination often demonstrates a focal area of tenderness. Not every bone is easily palpated; the pelvic bones, femur, talus, and midtarsal bones are notoriously difficult to examine. In the rear foot and mid-foot, a high level of suspicion must be present to reach the diagnosis. Imaging studies are helpful in the diagnosis. A bone scan will offer early sensitivity to stress reactions. MRI scans and x-rays can also be helpful. A CAT scan is the least useful imaging modality.

On the tibia, a horizontal line of tenderness is often the differentiating clinical sign from the vertical tenderness of medial tibial stress syndrome. However, spiral and vertical stress reactions can occur in the tibia. Immobilization in a pneumatic walker for four to six weeks or more is often helpful for tibial stress fractures and a variety of other stress injuries of bone. Calcaneal stress fractures may be suspected when there is tenderness upon lateral compression of the calcaneal body, rather than at the medial calcaneal tuberosity, or tenderness that is only plantar to the calcaneus.

Stress fractures of the tarsal navicular should be suspected when there is tenderness on the dorsal aspect that extends proximally to distally. In addition to tenderness, tenderness to percussion or to the vibrations of a tuning fork have been used as pathognomonic signs.

Diagnostic imaging includes radiographic evaluation, technetium-99 bone scan, and MRI. Often an injury is not visible on radiographic examination. Bone scintigraphy is considered sensitive, while MRI is

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considered to be both sensitive and specific. (Niva, Sormaala, et al. 2007) At early stages, the MRI shows marrow edema as an increased STIR signal and in fat-suppressed T2 images. On T1 sequences, a decreased signal is noted. (Stafford, Rosenthal, et al. 1986). As the injury progresses to a stage of increasing severity, a low signal fracture line and bone callus may be visible. A number of conditions may confound diagnosis and appear similar to stress fracture on certain imaging studies. In other cases, asymptomatic bone marrow edema may be visible on MRI. (Niva, Sormaala, et al. 2007)

Treatment

Conservative treatment works well for most stress-injuries of bone. Weight-bearing pain needs to be eliminated. With the elimination of pain, the forces should be sufficiently low for healing and remodeling to take place. Multiple authors have recommended the use of a pneumatic walker for tibial stress fractures.[62,63] This may be used alone or with crutches as needed. A cam walker, pneumatic walker, or low pneumatic walker may alleviate pain faster and be clinically superior to a post-operative shoe for stress reactions of the metatarsal area and for other foot stress reactions. An added benefit of the pneumatic walker is that it can be removed for exercise, bathing, and sleep.

Most lower extremity stress reactions take between eight and 17 weeks for recovery.[64] During recovery, one should guide the athlete to appropriate cross-training activity. Swimming, bicycling, and maintenance of upper body strength should be implemented. Lower extremity exercises should be chosen as appropriate.

A phased return to activity, allowing sufficient time for healing, is the key to a successful return to activity. In clinical practice, the author has found that weaning from the pneumatic walker seems to lessen the time to comfortable exit from the walker and prevent pain from returning and the necessity of returning to the use of the pneumatic walker.

Walking should start first building up from 20 minutes to 50 minutes. Running should start gently, with a slow build-up. After an adequate aerobic base has been achieved, a slow and gradual increase in other stressors may be added such as hill work, limited bursts of moderate speed, and later more intense and structured speed work.

Summary and Conclusion

Mechanics, mechano-biology, and tensegrity theory play a significant role in prevention of injury, maintenance of healthy tissue, and injury recovery. Research demonstrates that you cannot just add growth factors to injured tissue sites and hope for the best. Physical therapy, stretching, strengthening, and custom orthotics all have a basis in mechanics that correlate with mechano-transduction.

A recent study has confirmed that custom orthotics are helpful for a variety of overuse injuries.[65] Clinical observation suggests that the conformation of the shell to the foot may be more important to successful orthotic therapy than posting. Theories remain to be created and tested. Benno Nigg conceived his idea on muscle tuning as one possible mechanism for orthotic function.[66] Nigg felt that forces acting through the foot would create a "muscle tuning" effect that would dampen soft tissue vibrations and reduce the loading rate of bone, tendon, and cartilage in the leg. Certainly, this could lead to solving a portion of the puzzle. Tensegrity theory and mechanotransduction are other, fresh areas for investigation.

As clinicians, what is most important is getting our patients back on the road participating in their chosen sports. Strive to keep up with the clinical literature, make your own systematic observations, keep theory in mind, and go with what works best. George Sheehan often said, "we are all an experiment of one". Those "ones" make more sense when we add them up with large clinical studies. However, we must be prepared to make changes in therapy based on how that one patient in front of you is responding. ■

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EXAMINATION

Continuing Medical Education

See answer sheet on page 173.

1) The newly evolving science of mechanobiology derives from all of the following disciplines except:
- A) biochemistry
- B) biophysics
- C) astrophysics
- D) physiology

2) The term "tensegrity" coined by Buckminster Fuller derives from which of the following?
- A) tensional integrity
- B) tensor lighting
- C) tens therapy
- D) tension disorder

3) One feature of mechanotransduction is that there is relatively direct transmission of mechanical force via protein connectors from the cell membrane to the cell nucleus. This should work in which of the following manners:
- A) faster than the diffusion of growth factors
- B) slower than the diffusion of growth factors
- C) at the same speed
- D) at the speed of light

4) The cell
- A) has no essential structure, but is an amorphous blob
- B) is structured by its cytoskeleton, comprised of microtubules and microfilaments
- C) has unchangeable physical features
- D) can not alter any of its genetic functions which proceed at one rate throughout their lifespan

5) The Achilles tendon is subject to what forces while an individual is running?
- A) 2 times body weight
- B) 4 times body weight
- C) 8 times body weight
- D) 16 times body weight

6) The dry weight of tendon is made up of which of the following ranges of collagen?
- A) 10-20%
- B) 20-45%
- C) 30-55%
- D) 60-85%

7) Collagen type I is the most frequent collagen found in tendon. Which of the following structures are characteristic of Collagen type I?
- A) single strand
- B) double helix
- C) triple helix
- D) quadruple helix

8) Which of the following make up most of the metabolically active cells of tendon?
- A) tenoblasts
- B) chondrocytes
- C) tenocytes
- D) schwan cells

9) Tendinopathic tendon from overuse exhibits all of the following features with the exception of:
- A) increase in vascularization
- B) loss of tightly bundled collagen appearance
- C) increase in cellularity
- D) dramatic inflammation

10) The gastrocnemius crosses all of the following joints with the exception of which?
- A) knee
- B) midtarsal joint
- C) subtalar joint
- D) ankle joint

11) Calf muscle injuries can include all of the following structures with which exception?
- A) gastrocnemius
- B) soleus
- C) psoas
- D) plantaris

12) According to this review article, which of the following statements can be made on studies for the treatment of midsubstance Achilles tendinopathy?
- A) Eccentric stretching shows consistent results in large numbers of subjects, among all researchers, with more than 90% of subjects having good to excellent results
- B) Platelet rich plasma recently showed great promise for treatment of Achilles tendinopathy.
- C) There have been many studies with more than 3,000 subjects which unequivocally detail the optimal treatment of Achilles tendinopathy.
- D) Platelet rich plasma injection appears to be no better than saline injection in the treatment of Achilles tendinopathy.

13) Which of the following statements about bone is correct?
- A) Bone is an adaptable and changeable tissue. Mechanical, genetic, and hormonal factors come into play in the regulation of bone physiology.
- B) Bone is immutable. Once past childhood few changes to the skeletal structure are seen.
- C) Osteocytes derive from osteoclasts.
- D) Muscle strength and function has no effect on the density and characteristics of bone.

14) Researchers discussing what mechanical strain did to the function of bone function said which of the following catchy phrases?
- A) Bending bones break.
- B) Bending bones are like bending trees.
- C) Bending bones bends genes.
- D) Bending bones need braces.

Continued on page 172

Continuing Medical Education

EXAMINATION

(cont'd)

15) The four surfaces of bone that can undergo remodeling include all of the following with the exception of which?
A) Haversian system
B) periosteal
C) endosteal
D) osteoclastic

16) Training errors described by the phrase "the terrible too's" could be described as including all of the following with which exception?
A) too much
B) too soon
C) too often
D) too bad

17) Increased forces into the bones of the foot and leg which often lead to overuse injury is most likely caused by which of the following?
A) muscle fatigue from unaccustomed runs
B) cross training of swimming and biking
C) running every other day
D) running graduated amounts on packed dirt

18) In diagnosing stress injury to bone, which of the following would be the least often used and least useful imaging modality?
A) x-ray
B) MRI
C) CAT scan
D) bone scan

19) Which of the following statements can be made on risk of stress injury of bone based on studies described?
A) Low muscle cross sectional area decreases risk in female runners.
B) Low bone cross sectional area decreases risk in female runners.
C) Both low muscle cross sectional area and low bone cross sectional area are correlated with an increase in risk.
D) Both low muscle cross-sectional area and low bone cross-sectional area decrease risk.

20) Studies of bone stress injury have demonstrated which of the following?
A) Pain is a good prognostic indicator.
B) Pneumatic walking boots help speed the healing of tibial stress fractures.
C) Overtraining can lead to increased testosterone.
D) Lower estrogen decreases the risk of stress reaction of bone.

See answer sheet on page 173.

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EXAM #8/10
Overuse Injuries of Tendon and Bone: All the Small Things
(Pribut)

Circle:

1.	A	B	C	D	11.	A	B	C	D
2.	A	B	C	D	12.	A	B	C	D
3.	A	B	C	D	13.	A	B	C	D
4.	A	B	C	D	14.	A	B	C	D
5.	A	B	C	D	15.	A	B	C	D
6.	A	B	C	D	16.	A	B	C	D
7.	A	B	C	D	17.	A	B	C	D
8.	A	B	C	D	18.	A	B	C	D
9.	A	B	C	D	19.	A	B	C	D
10.	A	B	C	D	20.	A	B	C	D

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