Structure–function relationships of entheses in relation to mechanical load and exercise

H. M. Shaw, M. Benjamin

Cardiff School of Biosciences, Cardiff University, Cardiff, UK

Accepted for publication 7 February 2007

Entheses are regions of high-stress concentration that are commonly affected by overuse injuries in sport. This review summarizes current knowledge of their structure–function relationships – at the macroscopic, microscopic and molecular levels. Consideration is given to how stress concentration is reduced at fibrocartilaginous entheses by various adaptations which ensure that stress is dissipated away from the hard–soft tissue interface. The fundamental question of how a tendon or ligament is anchored to bone is addressed – particularly in relation to the paucity of compact bone at fibrocartilaginous entheses. The concept of an "enthesis organ" is reviewed – i.e. the idea of a collection of tissues adjacent to the enthesis itself, which jointly serve a common function – stress dissipation. The archetypal enthesis organ is that of the Achilles tendon and the functional importance of its subtendinous bursa, with its fibrocartilaginous walls and protruding fat pad, is emphasized. The distribution of adipose tissue elsewhere at entheses is also explained and possible functions of insertion-site fat are evaluated. Finally, a brief consideration is given to enthesopathies, with attention drawn to the possibility of degenerative changes affecting other regions of an enthesis organ, besides the enthesis itself.

What are entheses and why are they important?

An enthesis is the attachment of a tendon, ligament or joint capsule to bone. It is also called an insertion site, osteotendinous or osteoligamentous junction. Benjamin and McGonagle (2001) have coined the term "enthesis organ" to emphasize the point that structures adjacent to the enthesis itself also help to reduce stress concentration at the attachment site. Stress concentration is a key issue at an enthesis, because any insertion site represents the meeting point between two materials of very different physical properties (i.e. a "soft and flexible" tendon/ligament and a hard bone). Mechanical engineers know that such a recipe makes the region vulnerable to failure. Benjamin and McGonagle (2001) have also introduced the term "functional enthesis" to describe the wrap-around regions of tendons or ligaments (TL), where there is a change in direction around a bony or fibrous pulley (Vogel & Koob, 1989). This highlights the parallels between wrap-around regions and "true" entheses. However, the current review primarily focuses on the structure and function of entheses and enthesis organs and the reader is referred elsewhere for any further consideration of functional entheses (Benjamin & Ralphs, 1998; Benjamin & McGonagle, 2001). We have given particular emphasis in the current article to mechanical issues that relate to sport and exercise.

Functionally, entheses provide strong and stable anchorage that promotes musculo-skeletal movement with the necessary, concomitant joint integrity. However, they must serve as more than simple anchors, for in linking soft to hard tissue, entheses also need to minimize the risk of damage in the face of high levels of mechanical loading. They do this by facilitating the smooth transfer of force between soft and hard tissue. This can occur in either direction, and particularly in the context of sport it is important to remember that ground reaction forces can place enormous strain on TL entheses. An enthesis is thus a key link in any muscle–tendon–bone or bone–ligament–bone unit – and one that may experience considerably more stress than the TL itself. Curiously, however, Rijkelijkhuizen et al. (2005) have claimed that not all of the force generated by a muscle is transferred to bone via its connecting tendon. They argue that force transmission can continue even when a tendon is severed, provided that the connection between the epimysium and the epitendinous tissue is substantial and intact (Rijkelijkhuizen et al., 2005).
Despite the stress concentration at entheses, they are less likely to fail than other parts of the musculo-skeletal chain, because of their ability to withstand high mechanical loads. Nonetheless, they are vulnerable to overuse injuries and these present as a number of poorly understood, pathological changes that are collectively referred to as enthesopathies. Any such injury can have a significant impact on the ability of athletes to pursue their sport. Pathologies such as the epicondylloses (tennis and little league elbow), proximal patellar tendinopathy (jumper’s knee), a variety of Achilles insertional disorders and plantar fasciosis (“fasciitis” is probably a less appropriate synonym) are well known to sports medicine practitioners.

In the differential diagnosis of overuse injuries associated with sport and exercise, clinicians must recognize that entheses are also targeted in the seronegative spondyloarthopathies (SpA) (Benjamin and McGonagle, 2001). These are a diverse collection of chronic, autoimmune joint diseases that are among the most prevalent of rheumatic conditions. They include ankylosing spondylitis, reactive arthritis, psoriatic arthritis, and arthritis associated with inflammatory bowel disease. Similarly, Diffuse Idiopathic Skeletal Hyperostosis (DISH, formerly known as Forestier’s disease Cammisa et al., (1998)) is also characterized by excessive bone deposition at entheses that leads to the formation of bony spurs. Entheses are of particular concern to orthopedic surgeons who treat sporting injuries because of the common need to re-attach TL to bone – e.g. during the reconstruction of an anterior cruciate ligament. It is uniquely challenging to recreate the natural smooth transfer of load from TL to bone that typifies the healthy, original attachment site (Pendegrass et al., 2004). A variety of techniques have been pioneered surgically that attempt to do so, but most simply involve stapling the TL to the bone. More recently, however, various materials with viscous properties (e.g. hydroxyapatite) have been coated on the attachment site of the implanted TL (Pendegrass et al., 2004).

The reader concerned more broadly with the influence of exercise on the musculo-skeletal system should note that skeletal attachment sites have long been of interest to archaeologists in relation to physical activity. The focus of archaeologists has been exclusively on the characteristic markings left by entheses following skeletal maceration. The premise is that the appearance of dried bones conveys useful information about the lifestyle of ancient populations (Galera & Garralda, 1993). Greater physical activity (e.g. between males and females) is reflected by different enthesis markings. The constant stressing of a muscle from daily repetitive tasks of various types gives the archaeologist a skeletal record of habitual activity patterns and this has contributed to understanding a wide range of issues relating to ancient populations (social, cultural, labor, the development, and use of tools, etc. – Galera and Garralda (1993)).

**Enthesis structure**

**Macroscopic structure**

As TL approach bone, they flare out in order to increase the surface area of the attachment. A good example of this is the attachment of the Achilles tendon to the calcaneus or the combined insertion of the tendons of sartorius, gracilis, and semitendinosus onto the tibia. These three tendons constitute the pes anserinus (literally “duck’s foot”) because of their highly flared appearance. Both the Achilles tendon and the pes anserinus are also illustrative of the general principle that neighboring entheses often interconnect to form stronger and more stable attachments. Indeed, this may be reflected in their development – as with the Achilles tendon and the plantar fascia. In the fetus, these two structures are continuous over the posteroinferior aspect of the calcaneus, because both initially attach to the peri-chondrium, rather than to the cartilaginous anlagen itself (Snow et al., 1995). With growth, this continuity is certainly reduced, but may still be evident in adulthood (Milz et al., 2002) – although Snow et al. (1995) disagree. The direct continuity of one enthesis with another has also been observed between the insertion of the quadriceps tendon and origin of the patellar ligament (Toumi et al., 2006). Fibers from the former pass over the anterior surface of the patella (to which they also attach) to become directly continuous with the patellar ligament at its proximal enthesis. The convergence of entheses and the blending of attachment sites with adjacent fasciae is an adaptation for dissipating stress between one TL and another and thus reducing the risk of local failure. There are numerous, largely unnamed, fibrous connections between one TL and another in the immediate vicinity of their attachment sites. It may also account for why patients with enthesopathies can complain of pain and tenderness in areas adjacent to the principal enthesis involved. Thus, in considering cases of lateral epicondylody, the clinician should note that the attachment of the common extensor tendon merges imperceptibly with the enthesis of the lateral collateral ligament and that this in turn fuses with the annular ligament of the superior radioulnar joint (Milz et al., 2004).

On the other hand, there is a need to ensure that certain tendons attach to bone discretely in order to promote precise and highly intricate movements. It is interesting to consider whether this relates to a
particular propensity of tendons with small areas of bony attachment (relative to the size of the whole musculo-skeletal unit) for avulsion. A whole series of imaginatively named, avulsion fractures have been described in the hand and wrist (where TL often have small entheses) — e.g. mallet finger, coach’s finger, and gamekeeper’s thumb. However, it should be recognized that load may be reduced at a given attachment site (thus reducing the risk of avulsion) by dissipating the action of a single muscle belly over more than one tendon — e.g. with the digital tendons. In other regions of the body, stress dissipation can be promoted by a single tendon attaching to a number of bones. Thus, fibularis (peroneus) longus attaches to both the medial cuneiform and the first metatarsal, and tibialis posterior sends tendinous slips to every tarsal bone except the talus.

Microscopic structure

Classification of entheses

Because the pioneering, histological descriptions of entheses were largely published in German, one of the key early classifications distinguished between *die diaphysären-periostalen Ansätze* (“diaphysial–periosteal attachments”) and *die chondralen-apophysären Ansätze* (chondral–apophysal attachments) (Biermann, 1957; Knese & Biermann, 1958). However, these terms only refer to the attachments of TL to long bones and cannot be easily applied to other parts of the skeleton. Thus, more recently, broader terminologies have been devised to encompass the entire musculo-skeletal system. Benjamin and co-workers (Benjamin & McGonagle, 2001; Benjamin et al., 2002, 2006) have regarded entheses as being either fibrous or fibrocartilaginous, depending on the character of the tissue at the TL-bone interface [Fig. 1(a)–(c)]. Fibrous entheses are usually present where TLs attach to the diaphysis or metaphysis of a long bone — e.g. the tibial attachment of the medial collateral ligament (MCL) of the knee. They equate to the diaphysial–periosteal attachments of Biermann (1957) or to the “indirect” insertions of Woo et al. (1988). The former authors have sub-classified such entheses as “areal” or “circumscribed,” with the distinction relating to the surface area (i.e. the footprint) of the attachment. Areal entheses have fibers that flare out over a larger area than circumscribed attachments. Hems and Tillmann (2000) consider that regarding entheses as either fibrous or fibrocartilaginous is an oversimplification and argue that fibrous entheses can be sub-classified into “bony” or “periosteal” attachments to indicate whether the tendon inserts directly into the bone [Fig. 1(b)] or indirectly into it via the periosteum [Fig. 1(c)]. It should be recognized, however, that as development proceeds, periosteal entheses can become bony ones (Gao et al., 1996).

Fibrocartilaginous entheses (the “direct insertions” of Woo et al. (1988) or the chondral–apophysyal attachments of Knese and Biermann (1958) are more common than fibrous entheses and predominate at the epiphyses and apophyses of long bones and in the short bones of the carpus and tarsus (Benjamin et al., 1986). The archetypal fibrocartilaginous attachment is exemplified by that of the Achilles tendon on the calcaneus [Fig. 1(a) and (d)]. It should be noted, however, that the structure of a given enthesis can vary greatly from region to region. Hems and Tillmann (2000) emphasized this in their study of the attachments of the masticatory muscles, and both Benjamin et al. (1986) and Woo et al. (1988) have pointed out that what are termed fibrocartilaginous entheses are not cartilaginous in all regions. Thus, at the Achilles tendon insertion for example, the most superficial part of the attachment is purely fibrous (Benjamin et al., 2002). The significance of this in understanding the differential load transfer across the footprint of an enthesis has yet to be thoroughly explored, although it is recognized by Maganaris et al. (2004).

Although this review focuses on TL entheses, it is also important to remember that some muscles have fleshy attachments to bone and thus lack a tendinous link to the skeleton — although usually at one end only. Even at such attachment sites, however, muscle fibers do not anchor directly to the underlying periosteum, but attach to it via a small amount of connective tissue associated with the muscle fibers. These entheses correspond to the muscular or “fleshy” attachment sites of Biermann (1957).

Fibrocartilaginous entheses

Dolgo-Saburoff (1929) described a four-layered, bony attachment of the cat patellar ligament in which the zones defined were the ligament itself, uncalcified fibrocartilage, calcified fibrocartilage, and bone. The zonal concept, which is widely credited to have originated with this author, remains a cornerstone of descriptions today, although Benjamin et al. (2007) have pointed out that one or more of the zones may be locally absent. Cooper and Misol (1970) later showed that each of the zones has different characteristics, but emphasized how the zones can blend imperceptively with each other. Typically, the tendon or ligament region (i.e. the zone furthest away from the bone at an enthesis) is characterized by the presence of parallel bundles of collagen fibers, with rows of elongate fibroblasts lying between them. Within the zone of uncalcified fibrocartilage, these collagen fibers may become less obvious, as their staining properties are masked by
Fig. 1. Histological structure of entheses and the concept of an enthesis organ. (a) The fibrocartilaginous enthesis of the human Achilles tendon. Zones of calcified (CF) and uncalcified (UF) fibrocartilage are readily visible and large rounded fibrocartilage cells (FC) are conspicuous in the former. Note that a calcification front (the tidemark – T) separates hard from soft tissue, but that this is subtly different from the tissue boundary between tendon and bone (B). This boundary is marked by an irregular cement line (arrows). Scale bar = 100 μm. (b) The purely fibrous enthesis of pronator teres in the adult forearm. The dense fibrous connective tissue (DFCT) of the tendon approaches the bone at a very oblique angle and attaches directly to the bone – i.e. no periosteum is present. Scale bar = 200 μm. (c) The periosteal fibrous attachment of a horse ligament. Note that the ligament attaches indirectly to the bone via the thick periosteum. P, periosteum. Scale bar = 100 μm. (d) Low-power view of the enthesis organ associated with the human Achilles tendon. The enthesis organ comprises the enthesis itself (E), sesamoid (SF) and periosteal (PF) fibrocartilages, the retrocalcaneal bursa (RB) and the tip of Kager’s fat pad (FP). Note the virtual absence of compact bone at the enthesis. ST, superior tuberosity. Scale bar = 3 mm. (e) Higher-power view of the sesamoid and periosteal fibrocartilages in a region similar to that enclosed in the rectangle in (d). Note the presence of rounded fibrocartilage cells (FC). Scale bar = 100 μm.
those of the proteoglycan-rich, extracellular matrix (ECM), and the fibroblasts are replaced by fibrocartilage cells. These latter cells are more rounded and lie in lacunae, surrounded by a small amount of amorphous ECM. Again, they are typically arranged in longitudinal rows – reflecting their metaplastic origin from fibroblasts during development (see Benjamin & McGonagle, 2001 for further details). A basketweave arrangement of collagen fibers is sometimes evident within enthesis fibrocartilage and may spread the load of the TL over a broader area.

**Functional significance of uncalcified enthesis fibrocartilage.** The uncalcified fibrocartilage at an enthesis promotes a gradual change of elastic modulus that encourages the smooth transfer of load across the hard–soft tissue interface (Hems & Tillmann, 2000). It allows the gradual bending of TL collagen fibers as they approach the bone, in much the same way that a grommet on an electrical plug controls the bending of the lead that enters it (Schneider 1956). The “bending-control” function is supported by the correlation that exists between the quantity of uncalcified fibrocartilage at different entheses, and the range of insertional angle change that occurs with joint movement – the greater the angle change, the more fibrocartilage is present (Evans et al., 1990; Benjamin et al., 1991, 1992; Boszczyk et al., 2003). Fibrocartilage may also act as a “stretching brake” for tendons during muscular contraction (Knese & Biermann, 1958). In other words, it may prevent a tendon from narrowing as it elongates. Any significant narrowing too close to a bony interface may weaken the tendon attachment site. In all of these functions, fibrocartilage should primarily be viewed as a tissue geared toward resisting compression and/or shear (Benjamin & Ralphs, 1998).

Knese and Biermann (1958) highlighted the specialized nature of fibrocartilage cells and this issue has been addressed in much further detail by Benjamin and Ralphs (2004). These latter authors have commented on the transitional character of fibrocartilage and emphasized that the term fibrocartilage embraces a wide spectrum of tissues with properties intermediate between those of dense fibrous connective tissue and hyaline cartilage. However, it is the cartilage-like molecules in the ECM that are of particular importance in providing a TL with the ability to withstand compression (Milz et al., 2005). Such loading is an inevitable consequence of the changing insertional angle of a TL that accompanies joint movement. More recently, the orientation of collagen fibers at the insertion site has also attracted attention in relation to mechanisms for reducing stress concentration. Thomopoulos et al. (2006) demonstrated that a changing orientation of the collagen fibers from tendon to the bone results in changes to the predicted stress concentrations; this may therefore influence the cell phenotype and matrix production at the insertion.

**Tidemarks.** The layers of calcified and uncalcified fibrocartilage at an enthesis are separated by a calcification front [Fig. 1(a)] that is most commonly called the tidemark, but which in the older German literature was called die Grenzlinie. Occasionally (particularly in older people), the tidemark may be duplicated (Benjamin et al., 1986). Although a tidemark separates calcified from uncalcified fibrocartilage, collagen fibers in the two regions are continuous. Few authors have studied the importance of the tidemark at entheses, but the presence of a comparable boundary within articular cartilage has attracted greater attention. Redler et al. (1975) have raised the possibility that the tidemark tethers the perpendicularly orientated, collagen fibers in articular cartilage to reduce shearing stresses and Havelka and Horn (1999) have suggested that it prevents blood vessels from penetrating uncalcified cartilage. It is certainly a region of mechanical weakness at which horizontal clefts can develop both at TL entheses (Benjamin et al., 2007) and in articular cartilage (Kumar et al., 1991). Furthermore, in both tissues, it is the interface at which the soft tissues fall away from the hard ones, during the preparation of an anatomical skeleton (Benjamin et al., 1986). It is also pertinent to note that the presence of multiple tidemarks in articular cartilage has long been associated with osteoarthritis (Lane & Bullough, 1980) and that tendon entheses too can show osteoarthritic-like degenerative changes and multiple tidemarks (Rufai et al., 1995; Benjamin et al., 2007).

The exact structure of a tidemark is difficult to define. Havelka and Horn (1999) have described a wide spectrum of appearances, from fibrillated to granular, and pointed out that the tidemark may be ill-defined (particularly if the tissue is pathological), may vary with age and may change with the degree of loading. Lyons et al. (2005) believe that the tidemark in articular cartilage is formed by two juxtaposed laminae with differing biochemical characteristics. They suggest that it inhibits hydroxyapatite crystal formation and growth after musculo-skeletal maturity. In this way, the cartilage is protected from progressive mineralization. Clearly, this could also apply to the fibrocartilage at entheses and it may help to bear this in mind when considering the significance of multiple tidemarks that can be a feature of degenerative insertional tendinopathies. Curiously, Zoeger et al. (2006) have found that tidemarks in articular cartilage have a particular propensity for accumulating lead, although the significance of this is unclear. The calcified (fibro)cartilage cells immediately deep to the tidemark have characteristics similar to those in the neighboring uncalcified region and
their viability has been confirmed by a number of authors, as reviewed in articular cartilage by Havelka and Horn (1999).

Subchondral bone plate. Although the tidemark is the mechanical boundary of an enthesis, it is subtly distinct from the tissue boundary – i.e. the interface between TL and bone (Hems & Tillmann, 2000). This is represented by a cement line [Fig. 1(a)]. In sharp contrast to the straightness of a normal tidemark, the cement line is highly convoluted, and the increased surface area it creates between TL and bone promotes firm anchorage and resistance to shear. As Hems and Tillmann (2000) have explained, the two interfaces have conflicting mechanical demands and thus need to be spatially distinct. The tidemark has to be as straight and smooth as possible at a healthy enthesis so that movement of soft tissue over hard tissue does not result in damage to the former. On the other hand, a straight boundary between hard and soft tissues does not make for the most secure mechanism of attaching a TL to a bone. Anchorage is thus better promoted by increasing the surface area of contact between the two tissues. Hence, the arrangement is that the terminal part of the TL is represented by a zone of calcified fibrocartilage that has an irregular interface (i.e. a cement line) with the underlying bone. The irregularity gives good resistance to shear – essential because TLs pull on bone from typically oblique angles. Whether or not there is significant continuity of collagen fibers across the cement line (i.e. from TL to bone) at a fibrocartilaginous enthesis is debatable. The traditional view is that TL attach to bone via “Sharpey’s fibers” and indeed, such fibers are obviously present at certain fibrous entheses (Hems & Tillmann, 2000). However, Benjamin et al. (2007) point out that compact bone may be virtually absent at even the largest of fibrocartilaginous entheses and that the cortical shell is often no more than a continuum of spongy bone trabeculae. Thus, there would seem to be insufficient cortical bone at the attachment site itself [see Fig. 1(d)], to accommodate many/any deeply penetrating collagen fibers. It is worth noting, however, that Haines and Mohuiddin (1968) suggest that the fibers that cross the tidemark between uncalcified and calcified fibrocartilage at TL entheses could be considered as equivalent to Sharpey’s fibers, because calcified fibrocartilage can be viewed as metaplastic bone. Although such considerations are valid, Milz et al. (2002) suggest that it is the highly interdigitating nature of the calcified fibrocartilage zone of the inserting TL and underlying bone that is of fundamental importance in promoting attachment.

Molecular composition of enthesis fibrocartilage. The reader is referred to earlier reviews by Benjamin and McGonagle (2001) and Milz et al. (2005) for a comprehensive account of the great variety of different molecules that have been found at entheses. Clearly, the ECM molecules in enthesis fibrocartilage must play an important role in force transfer at attachment sites, and the type of molecule present is directly related to the mechanical demands at the interface. This is the basic premise developed in the extensive monograph of Milz et al. (2005). They emphasize how the expression of the glycosaminoglycans (GAGs), chondroitin – 4 and 6 – sulfate is elevated at fibrocartilaginous entheses, reflecting the compressive loading to which the attachment site is subject. These GAGs are usually associated with aggrecan – a large, aggregating proteoglycan that is a major constituent of the ECM in hyaline articular cartilage. Aggrecan is a hydrophilic molecule that
imbibes water and thus allows a TL to withstand compression (Yoon & Halper, 2005). It is probably the aggrecan content of entheses that accounts for the ability of the uncalcified fibrocartilage to dissipate collagen fiber bending and prevent TL narrowing from occurring too close to the bony interface, under load. Other small, leucine-rich, proteoglycans such as decorin, fibromodulin and lumican have also been detected immunohistochemically in enthesis fibrocartilage. They may have an important role in regulating collagen fibril formation and thus determining the tensile strength of the TL (Milz et al., 2005). The importance of cartilage-like molecules in tendons has been highlighted by Corps et al. (2004, 2006). They demonstrate that levels of aggrecan and biglycan in painful tendinopathy are increased and may reflect the change in mechanical loading at the site of the lesion, leading to a more cartilage-like phenotype of the tissue. Such an increased expression of these proteoglycans would also be expected to occur at entheses, as changes in mechanical loading are also experienced here in injured tendons. These changes may in turn cause a further alteration in the mechanical loading and consequently trigger a vicious cycle of increased pathology (Maffulli et al., 2006).

While type I collagen generally predominates in the midsubstance of a TL, and in bone, type II collagen (the typical collagen of cartilage) is only characteristic of the fibrocartilage zones (Milz et al., 2005). Although types III and IV collagen show no significant regional variations across the TL-bone unit, the expression of the latter does vary between the mid-substance of the TL and the fibrocartilage zones. In the TL itself, type IV collagen is found throughout the ECM, while in the fibrocartilaginous regions it has a more restricted and pericellular distribution. This suggests that type IV collagen has different matrix-binding functions in these regions (Waggett et al., 1998). Type III collagen has the ability to form heterotypic fibrils with types I and V collagen and is believed to play a role in controlling fibril diameter (Birk & Mayne, 1997; Waggett et al., 1998). Type X collagen has also been identified at entheses (within the zone of calcified fibrocartilage) and is thought to be important in controlling calcification (Fujioka et al., 1997). Interestingly, Kruzynska-Frejtag et al. (2004) have recently demonstrated the presence of a cell-adhesion molecule called “periostin” at the periodontal ligament enthesis that may also be involved in controlling mineralization. They suggest that high levels of periostin present at hard–soft tissue interfaces may prevent ligament cells near the soft–hard tissue boundary from differentiating into an osteogenic phenotype. In other words, the molecule helps to maintain the ligament as a non-mineralized tissue.

It would thus be of interest to know whether periostin is expressed at other entheses and whether a reduction in its expression is associated with the spread of mineralization into soft tissues. Finally, it must be acknowledged that we know little about the turnover of any enthesis ECM molecules, but in the rest of the TL, it seems that men have elevated levels of collagen synthesis following exercise compared with women (Miller et al., 2007). This has been related to the greater incidence of exercise-related musculo-skeletal injuries in women.

**Fibrous entheses**

Fibrous entheses have attracted far less interest than fibrocartilaginous attachments, probably because they are less frequently involved in enthesopathies. Nevertheless, a number of large and powerful muscles (e.g. deltoid, pectoralis major and latissimus dorsi; Benjamin et al., 1986) and important ligaments (e.g. the knee joint MCL; Woo et al., 1988) have fibrous entheses. The footprint of fibrous entheses is generally broad and this helps to dissipate the stress over a wide area and minimize stretching.

As outlined earlier, there are two forms of fibrous entheses – those that attach directly to cortical bone and those that attach indirectly to it via the periosteum [Fig. 1(b) and (c)]. Following closure of the growth plate, a periosteal fibrous enthesis can become a bony one, although some TL attach to the periosteum throughout life (Hems & Tillmann, 2000). It is important to recognize that the initial perioosteal attachment of a metaphyseal TL to a long bone allows the TL to migrate as the bone lengthens, so that the relative position of the ligament remains unchanged. This is because theperiosteum can grow interstitially, but the bone itself cannot – it can only grow by appositional means. A perioisteal, fibrous enthesis is inevitably weaker than a bony one and this is a fact that should be recognized by those concerned with coaching young children in sport, for it has a bearing on the loading of entheses during puberty in athletic children.

**The enthesis organ concept and its relevance in sports medicine**

Benjamin and McGonagle (2001) coined the term “enthesis organ” to denote a collection of structures adjacent to the attachment site itself that are functionally associated with the enthesis and that also play an important part in reducing stress concentration at the soft–hard tissue interface. The concept of an enthesis organ explains why patients may present with symptoms adjacent to an enthesis as well as at the enthesis itself.
The archetypal enthesis organ is that of the Achilles tendon [Fig. 1(d)], which Canoso (1998) described as the “première enthesis.” Canoso was aware of the contribution of neighboring structures to the role of the enthesis itself and had made particularly pertinent observations on the functions of Kager’s fat pad that protrudes into the retrocalcaneal bursa (Canoso et al., 1988). The triangular tip of this fat pad, the retrocalcaneal bursa itself, and the fibrocartilages that form its walls collectively constitute the enthesis organ of the Achilles tendon, together with the enthesis itself [Fig. 1(d)]. The two fibrocartilages in the bursal walls comprise a variably thick, periosteal fibrocartilage on the superior tuberosity of the calcaneus, and a sesamoid fibrocartilage within the deep surface of the opposing tendon [Fig. 1(e)]. They are an adaptation to resist compression and/or shear when the foot is dorsiflexed and the tendon is brought in contact with the tuberosity. The fluid-filled bursa facilitates a change in insertional angle between the tendon and the bone during foot movements. By analogy with synovial joints, the presence of hyaluronan within the bursa might be expected to reduce the coefficient of friction substantially and thus prevent the buildup of heat. Bursal fluid may also be important as a source of nutrients and oxygen for the avascular fibrocartilages.

In understanding the general concept of an enthesis organ, the reader should note that the bone immediately adjacent to the Achilles tendon enthesis (i.e. the superior tuberosity) acts as a mini pulley for the tendon and that contact between tendon and pulley reduces stress concentration at the enthesis itself, albeit, this is at the expense of increasing wear and tear in the contact zone. The corollary is that the surgical removal of a prominent superior calcaneal tuberosity in patients with Haglund’s deformity will inevitably increase the stress concentration on the enthesis itself. When the contact zone between tendon and tuberosity is no longer present (i.e. when the tuberosity is removed by the surgeon), none of the tensile loading placed on the Achilles tendon can be dissipated as compressive loading on the bone, adjacent to the insertion site. Instead, all of the loading on the tendon is transferred directly to the enthesis itself. It is thus conceivable that if the patient is an athlete who loads their Achilles tendon heavily during the course of their sport, this might produce a new set of problems – a possibility that merits further consideration. Evidence of increased wear and tear in the tendon–bone contact zone adjacent to the Achilles tendon enthesis is common in the walls of the retrocalcaneal bursa of elderly individuals (Rufai et al., 1995).

It should be noted that as dorsiflexion begins and the Achilles tendon presses against the tuberosity, the insertional angle of the tendon is not altered with further foot movement. Similarly, even the most cursory of observations on a living foot shows that as the foot is plantarflexed, any large change in insertional angle is greatly reduced by the controlling influence of the deep fascia in the lower part of the leg. This acts as an unheralded retinaculum to prevent bowstringing of the Achilles tendon and should probably be added to the list of structures that form part of its enthesis organ. Whether it is involved in Achilles tendon sheath problems is a question that has not been addressed. It is difficult to distinguish the two structures in a dissection of the terminal part of the Achilles tendon.

Enthesis organs are found elsewhere in the body and many sites have been listed by Benjamin et al. (2004a, b). Because of its relevance to the sports medicine practitioner, the attention of the reader is drawn to the presence of an enthesis organ at the talar end of the anterior talofibular ligament of the ankle joint – a ligament commonly damaged in ankle sprains. The contact that occurs between the ligament and the talus in a plantarflexed and inverted foot, immediately adjacent to the attachment site, is associated with the presence of a sesamoid fibrocartilage near the deep surface of the ligament (Kumai et al., 2002). This is likely to reduce the stress concentration at the enthesis itself. Kumai et al. (2002) relate the presence of this distally located enthesis organ in the ligament to the greater tendency of the proximal enthesis to avulse in ankle sprains. Clearly, however, differences in bone density between the talar and fibular entheses are also important.

In generalizing from the specific features of the Achilles tendon enthesis organ to concepts that apply elsewhere in the body, it is important to recognize that TLs often attach to bone near tuberosities or are sunken into pits. In either case, the TL enthesis is sited below the level of the adjacent bone. The presence of a tuberosity is exemplified by that at the insertion of biceps brachii and patellar tendons, and the presence of a pit by the attachment of the tendon of popliteus and by the collateral ligaments of the interphalangeal joints. It should be noted that wherever a TL sinks into a pit at its attachment, the adjacent bone surface can also act as a pulley, dissipating stress away from the attachment site itself.

Kager’s fat pad is an important part of the Achilles tendon enthesis organ that is often ignored. It is also known as the retromalleolar or pre-Achilles fat pad and it has a number of functions. Its tip moves in and out of the bursal cavity during plantar and dorsiflexion like a variable plunger (Canoso et al., 1988; Theobald et al., 2006). This minimizes pressure changes in the bursal cavity and ensures that the space is a potential, rather than a real one, at a healthy attachment site. The fat pad may also pre-
vent adhesions from developing between the tendon and the bone. All these observations on the function of this region of adipose tissue, together with other comments on its significance detailed below, should be of interest to surgeons who perform any operation that disturbs Kager’s triangle.

According to Theobald et al. (2006), Kager’s fat pad has three distinct regions: an Achilles-associated part (which is enclosed within the paratenon of the Achilles tendon), the flexor hallucis longus (FHL)-associated region (which is partly enveloped by the tendon sheath of FHL) and a distal bursal wedge or tip that protrudes into the bursal cavity. The movement of the fat pad in and out of the bursa is promoted both by pushing (contraction of FHL) and by pulling (it is sucked into the bursa to prevent the volume from increasing during the upward motion of the calcaneus during plantarflexion). In addition, the fat pad cushions the deep surface of the Achilles tendon offering protection to the blood vessels that enter it, and prevents the tendon from kinking during plantarflexion (Theobald et al., 2006). It may also have a proprioceptive role in monitoring changes in the insertional angle of the tendon during foot movement (Benjamin et al., 2004a, b; Shaw et al., 2005). The latter hypothesis is supported by the demonstration of an abundant sensory nerve supply within the fat pad (Shaw et al., 2005). Finally, as the fat pad contains peptidergic nerve fibers involved in nociception, it may be a source of pain in enthesopathies (Shaw et al., 2005). This could be mediated either through direct stimulation of nerve endings or by neurogenic inflammation. It is important to recognize that in the rat at least, the fat pad is the only part of the normal Achilles tendon enthesis organ that is innervated (Shaw et al., 2005). However, in humans, nerve fibers often accompany blood vessels in the vascular invasion of entheses that so often occurs in elderly individuals (Benjamin et al., 2007).

The presence of adipose tissue at other entheses is also common. However, its significance is often misinterpreted and many authors automatically equate it with TL degeneration. Although Benjamin et al. (2004a, b) agree that fat in TL may be pathological, they also argue for a variety of normal functions of fat at or near entheses. They have shown that adipose tissue is present not only at the insertional angle of many entheses but also in the epitenon and endotenon near the attachment site (Benjamin et al., 2004a, b). The fat is often innervated and may have a mechanosensory role. Endotenon fat is particularly characteristic of certain entheses where the TL flares out [e.g. fibularis (peroneus) longus insertion and the tibial attachment of the ACL]. It may thus contribute as a space filler and/or promote the independent movement of fascicles (Benjamin et al., 2004a, b).

**Enthesopathies**

Despite the adaptations that occur at entheses for preventing wear and tear, they are still prone to pathological changes. Overuse injuries in particular are common in athletes and account for a high proportion of all sports injuries. They are best termed “enthesopathies” (a term that embraces both tendons and ligaments), but have also been called “enthesiopathies,” “insertional tendinopathies,” or “insertional tendinoses” – although the last two can of course only be applied to tendons. The reader should also note that some authors use a more general pathological term, which applies to a whole tendon or ligament, when discussing enthesopathies. “Achillodynia” for example, covers the whole spectrum of Achilles tendon problems commonly reported in athletes and the term may disguise the fact that an author is at least partly considering enthesopathies. The term “enthesitis” may be appropriate for some enthesopathies (e.g. in patients with SpA), but carries with it the implication that an attachment site is inflamed (the suffix _itis_). The reader should note therefore that the current consensus view is that most overuse injuries at entheses are degenerative rather than inflammatory. Where inflammation does occur, it may be a secondary change related to tissue damage and repair. This suggestion was made by Rufai et al. (1995) in relation to retrocalcaneal bursitis. They suggested that the synovial inflammation that is characteristic of the bursitis may not be a primary event, but a secondary change triggered by degeneration (fissuring, fragmentation and calcification) of the periosteal and sesamoid fibrocartilages that line the bursal walls and form part of the Achilles tendon enthesis organ – i.e. retrocalcaneal bursitis is primarily a problem related to fibrocartilage degeneration. This is also a reminder that the clinical symptoms of an enthesopathy need not necessarily affect only the enthesis.

The etiology of enthesopathies is often unclear, although as with tendinopathies in general, both intrinsic and extrinsic factors are involved. The former include anatomical variations, malalignment problems, muscle imbalance, or weakness and flexibility issues (Wilder & Sethi, 2004). The latter may relate to changes in training programs (including terrain, mileage coverage, duration, and intensity of training), inappropriate footwear, poor technique, or equipment (Wilder & Sethi, 2004). Maganaris et al. (2004) have made the interesting suggestion that some “overuse” insertional injuries would be better regarded as “underuse” injuries. They argue that parts of entheses may be stress shielded, so that when increased loading occurs, that particular region of the attachment site is unable to adapt sufficiently. They point out that the stress-shielded area is often

---

Tendon and ligament entheses

---
subject to greater compressive (rather than tensile) loading than the rest of the enthesis. Such regions are characterized by fibrocartilage (Benjamin & Ralphs, 1998) – a tissue that can show a variety of pathological changes at the certain entheses – e.g. that of the Achilles tendon (Rufai et al., 1995). Maganaris et al. (2004) suggest that tensile loading at entheses is non-uniform and it is the less heavily loaded regions that are the most vulnerable. Commonly, these are on the joint side of an attachment site – e.g. in rotator cuff problems, jumper’s knee and Achilles insertion disorders. Certainly, so-called “fibrocartilaginous entheses” are of non-uniform composition and are purely fibrous in some parts of the enthesis (Benjamin et al., 1986; Woo et al., 1988). This is likely to reflect regional differences in tensile loading. It must be remembered, however, that an increase in compressive loading in what is regarded as a “stress-shielded” site of an enthesis may lead to degenerative changes that parallel those in osteoarthritic articular cartilage (Rufai et al., 1995). These may contribute to the histopathological basis of overuse injuries. It should also be noted that Toumi et al. (2006) highlight regional differences in trabecular architecture at the patellar enthesis of the patellar tendon. As Wolff’s law dictates that mechanical stress governs the architecture of cancellous bone, Toumi et al. (2006) suggest that the medial part of the attachment site is subject to greater tensile loading than the lateral – it is this region of the enthesis that is most typically associated with jumper’s knee.

Enthesopathies can affect a wide variety of different TLs and among the most common (and relevant to sport) are those that affect the Achilles tendon, patellar tendon, quadriceps tendon, supraspinatus and the common extensor and flexor tendons of the forearm (Khan et al., 1999). In addition, it should be noted that Fairclough et al. (2006) have suggested that iliotibial band (ITB) syndrome could be viewed as a form of enthesopathy. It is a well-recognized overuse injury that is common in runners and cyclists and is characterized by pain and tenderness over the lateral epicondyle of the femur when the knee is flexed to 30°. ITB syndrome is traditionally believed to be caused by repetitive friction between the band and the lateral epicondyle of the femur, when the ITB “rolls over” the epicondyle during knee movement. However, Fairclough et al. (2006) point out that the ITB cannot move in an anterior–posterior direction as the knee is flexed, because the band is firmly anchored to the distal part of the femur – i.e. it has an enthesis in the region of the lateral femoral epicondyle. They have suggested that the antero-posterior “movement” of the band is actually an illusion created by a sequential shifting of tensile load from anterior to posterior ITB fibers, during knee flexion. Their magnetic resonance imaging (MRI) data suggest that the tract moves in a medial–lateral direction during knee flexion. This creates a change in the insertional angle of the femoral enthesis of the ITB. They have also demonstrated the presence of highly vascularized and innervated adipose tissue between the ITB and the lateral epicondyle that is the equivalent of the insertional angle fat at many entheses Benjamin et al. (2004a, b). Evidently, the fat must be compressed by any medial–lateral movement of the ITB. Intriguingly, there are MRI signal changes in this fat in patients with ITB syndrome, and Fairclough et al. (2006) consider this to be of key importance in understanding the pain and edema associated with ITB syndrome.

Finally, it should be noted that Knobloch et al. (2006) have demonstrated a significant increase in the microcirculatory blood flow at painful Achilles tendon entheses. This is in-line with earlier studies which have shown that angiogenesis occurs in painful mid-portion tendinopathies (Alfredson et al., 2003; Alfredson & Ohberg, 2005) and has led to the suggestion that enthesopathies or tendinopathies could be treated with agents that affect neovascular development (Ohberg & Alfredson, 2002).

Enthesophytes (bony spurs)

Particular mention is made of bony spurs (enthesophytes) as they are commonly found in athletes – especially at the attachment of the Achilles tendon, common extensor origin and plantar fascia. The molecular pathways that lead to their formation have not yet been clearly elucidated, although loss of noggin (an antagonist of bone morphogenetic protein expression) can induce ectopic bone formation in ankylosis (Lories et al., 2006). Some spurs may exceed 1 cm in length (Maffulli et al., 2004), but even large ones may not be symptomatic. However, spurs may be associated histologically with evidence of degenerative change elsewhere at the enthesis (Rufai et al., 1995). Enthesophytes in the Achilles tendon must be distinguished from what are simply areas of soft tissue calcification at the enthesis (Rufai et al., 1995). The term “enthesophyte” implies specifically that ossification has extended from the bone into the TL at the attachment site, whereas soft tissue calcification merely means the deposition of calcium salts. It is commonly reported in tendons as calcifying tendonitis or tendinopathy and is more typical of males than females at the attachment of the Achilles tendon (M. Benjamin, unpublished observations). It should be understood that calcification accompanies ossification, but can occur in its absence – this is a point of common confusion among those new to the field. The distinction between soft tissue calcification at an enthesis and bony spur formation can easily be
made in histological sections, but may also be made radiologically (Rufai et al., 1995).

**Perspectives**

Overuse injuries at tendon or ligament attachment sites (entheses) are common and can seriously jeopardize a subject’s ability to pursue their sport. However, there is often a lack of awareness among sports medicine practitioners about many fundamental aspects of the structure–function relationships of insertion sites that are essential for understanding the basis of enthesopathies. In particular, the tendency of one enthesis to interconnect with another and the concept of an “enthesis organ” (a collection of structures adjacent to entheses, which, together with the attachment site itself, serve to reduce stress concentration at the hard–soft tissue interface) have a number of implications for understanding (a) why symptoms associated with enthesopathies may be diffuse and (b) why the surgical removal of a structure close to an enthesis e.g. the superior tuberosity of the calcaneus may alter the mechanics of the enthesis itself. It is argued that a good understanding of the structural adaptations of entheses, and an appreciation that one attachment site may be very different from another, should be helpful to an orthopedic surgeon concerned with the reattachment of a tendon or ligament to a bone.

**Key words:** tendons, ligaments, osteotendinous junction, enthesopathy, fibrocartilage, overuse injuries.

**Acknowledgement**

We wish to thank Andrew Bathe of the Rossdales Equine Hospital, Newmarket, UK for supplying the horse tissue from which Fig 1(c) was taken.

**References**


Shaw & Benjamin


