REVIEW OF CURRENT KNOWLEDGE OF PATHOLOGY AND TREATMENT OF TENDINOPATHIES
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Abstract

Tendon pain has been considered either an inflammatory result of injury or a degenerative process, (Khan, Cook, Kannus, Maffulli, & Bonar, 2002) but further studies are revealing that it is a complex combination of the two, or a failed healing response. (D'Addona, Maffulli, Formisano, & Rosa, 2017) Some tendon problems are the result of factors external to the tendon, such as excessive demands or mechanical abrasion. At least initially, these are largely inflammatory in nature and may appropriately be termed tendinitis. Reducing inflammation may be an appropriate part of treatment. Other tendon problems occur without obvious injury in inactive individuals. These are mostly degenerative in nature, and have been termed tendinosis to indicate that a non-inflammatory process is at work. If either of these processes is allowed to continue, there will eventually be an arrest of healing. Osti (Osti et al., 2017) (Bhabra et al., 2016) Macroscopic tears may result. By recognizing that there are three general types of tendon pathology ---inflammatory, degenerative, and arrested healing -- treatment can be modified to match the defect.

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Introduction

Tendon pain has been considered either an inflammatory result of injury or a degenerative process, (Khan et al., 2002) but further studies are revealing that it is a complex combination of the two, or a failed healing response. (D'Addona et al., 2017) Thus by recognizing that there are three general types of tendon pathology ---inflammatory, degenerative, and arrested healing -- treatment can be modified to match the defect.

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Tendonitis
Some tendon problems are the result of factors external to the tendon, such as excessive demands or mechanical abrasion at some contact point, such as the supraspinatus tendon on the acromion. At least initially, these are largely inflammatory in nature, and may appropriately be termed tendinitis. There is an increase in inflammatory cytokines such as TNF-α and IL-1β, which stimulates interleukin 6, all of which induces the acute phase response. These injuries may heal relatively quickly if the offending mechanism is removed and the natural reparative mechanisms can return the tendon to normal. Reducing inflammation may be an appropriate part of treatment.
These conditions have been termed tendinosis to indicate that a non-inflamatory process is at work.

Tendinopathy
Other tendon problems occur without obvious injury, in inactive individuals, and/or at the non-tensile portion of a tendon. (Almekinders, Vellema, & Weinhold, 2002) These are mostly degenerative in nature. Histological studies show few inflammatory cells. There is disordered synthesis of collagen, increase in ground substance, and mucoid degeneration. Caspace induces other interleukins. Vascular endothelial growth factor may promote the proliferation of tenocytes as well as the release of cyclo-oxygenase-2 and prostaglandins implicated in the insurgence of pain. On a macroscopic level there is sometimes more damage from crimping or kinking which results in compression damage to the fibers, as opposed to tearing from excess tensile force. (Herod & Veres, 2017)

Arrested Healing
If either of these processes are allowed to continue, there will eventually be apoptosis of the tenocytes and an arrest of healing. Osti (Osti et al., 2017) (Bhabra et al., 2016) There is neovascularization and nerve ingrowth, neither of which are functional but are likely pain generators. (Spang & Alfredson, 2017) At this stage, management becomes even more difficult, macroscopic tears may result, and surgery may be necessary.
Treatment

Inflammation

Inflammation causes initial swelling and degradation, but is also necessary to drive ultimate repair and remodeling. (Dakin et al., 2015)

The healing phase actually begins early with heat shock proteins produced in response to stress, which serve to protect against the insult of caspace induced apoptosis. They also produce a state of resistance to subsequent stress in the cell, as well as augment recovery. Inflammatory cytokines dampen the apoptosis of tenocytes, and thus it is important to not block all cytokines. (Osti et al., 2017)

As we have come to appreciate the different phases or forms of tendinopathy, and study more carefully the effects of treatments, some standard interventions are proving to be rather ineffective, and other new or underappreciated options are more promising.

Relatively Ineffective Treatments Rest

If tendon injury has a clear inciting factor and it occurs in a young patient, relative rest may avoid further insult to damaged tissue, minimize pain, and allow the healing processes to predominate. But even here, total rest is not the best; protected return to activity and carefully titrated exercise improves tendon repair.(Abat et al., 2017; van den Bekerom et al., 2012)

ICE

Cry therapy has a long history of use in the treatment of musculoskeletal conditions, especially in Western sports medicine. It reduces inflammation in acute injury, reduces acute pain, and causes vasoconstriction of the neovascularization, and thus provides pain relief, and possibly some reversal of the maladaptive processes. A large advantage is that it likely does not impede healing processes if used in the reparative phase.(Vieira Ramos et al., 2016) But there actually are no good studies showing benefit in medium to long term return to activity.(Bleakley, McDonough, & MacAuley, 2004; Hubbard & Denegar, 2004; van den Bekerom et al., 2012) This may be a result of
the difficulty designing a study with blinded controls, but is does remind us to constantly evaluate the effectiveness of traditional treatments.

**Corticosteroids**
The lack of inflammatory cells in degenerative and arrest of healing tendinopathies gives indication why corticosteroids have limited benefit. There is some evidence that corticosteroids--systemic and injected--may provide initial pain relief, and thus why clinicians have used them with apparent benefit for decades. But there is actually little to no evidence for long term benefit. (Coombes, Bisset, & Vicenzino, 2010) If indeed some inflammatory cytokines are needed to reverse degeneration and induce repair, (Dakin et al., 2015; Urso, 2013)corticosteroids are counterproductive. Evidence is mounting that they also have a mildly deleterious effects on most tissue, thus the risk/benefit ratio is generally unfavorable. (Abat et al., 2017; McAlindon et al., 2017; Mohamadi, Chan, Claessen, Ring, & Chen, 2017; Olaussen, Holmedal, Mdala, Brage, & Lindbaek, 2015)

**Anti-Inflammatories**
Inflammation does cause damage and pain, but it also promotes healing. Thus, while oral NSAIDs are useful for pain management, but may actually interfere with long term healing. (Urso, 2013) Some studies also show that they actually do not reduce inflammation as much as thought. (Vella et al., 2016) They have a place in the treatment plan as long as they are used for pain management. If a patient finds they do not help with pain, they must be stopped.

**What Does Help?**
If tendinopathy is a degradative process or arrested healing, it is necessary to stimulate the tenocytes to perform a functional repair of the tissue. There are many ways to do this, but presented here are three that are applicable in most settings, and two interventional non-surgical options that show promise.

**Eccentric Exercise**
This special type of exercise has been promoted in the last decade as the foundation of restoring tendon tissue structure and function. (Alfredson,
Pietila, Jonsson, & Lorentzon, 1998) There is fairly good evidence for this in achilles and patellar tendinopathy, but not for other sites. (Dejaco, Habets, van Loon, van Grinsven, & van Cingel, 2017) The mechanism is unclear. It may work by reducing the crimping that occurs at the end of the contraction/stretch cycle of concentric exercise. Or it may be that there is neuromuscular adaptation that “smooths” mini contractions or increases muscle and tendon stiffness. Perhaps counterintuitively, increased stiffness is protective from injury.(O'Neill, Watson, & Barry, 2015)

**Manual Stimulation of the Tissue**

Irritation or stimulation of the tissue with deep massage, either with hands or tools, are commonly used, although clear evidence is not available yet.(Cheatham, Lee, Cain, & Baker, 2016) The mechanism is unclear, but it may be related to disruption of the scar tissue and neovascularization, release of adhesions, as well as stimulation of tenocytes and growth factors.

**Dry Needling**

This form of therapy usually entails the insertion of solid bore needle into myofascial trigger points, but it can also include the insertion of needles at remote areas, around nerves, or around a tendon, all without the injection of any therapeutic substance.(Kubo et al., 2010) There is overlap with acupuncture,(Dorsher, 2008) although this is a point of controversy. The evidence for positive effect is not yet of high quality.(Gattie, Cleland, & Snodgrass, 2017).

**Orthobiologics**

Of great interest lately are the regenerative therapies such as injection of platelet rich plasma or stem cells into the pathological tissue. This has been made possible by advances in point of care ultrasound, which allow precise placement of these injections. Knee Surgery and Arthroscopy is that “the use of US imaging in the diagnosis and treatment of tendinopathies should be mandatory.”(Abat et al., 2017) But in spite of these therapies having been available for several years now, the evidence for efficacy beyond placebo while promising,(James et al., 2007) is limited.(Coombes, Connelly, Bisset, & Vicenzino, 2016) Admittedly
evidence will be difficult because there is such a variety of preparations, and the placebo injections themselves are fairly therapeutic. Fenistration of the tissue by the needle may provide much of the stimulation of tenocytes needed to start regeneration. (Chiavaras & Jacobson, 2013) If so, this will be very useful because while treatments such as stem cell and platelet rich plasma injections are very costly, simple fenistration of the tendinopathic tissue can be done by any clinician familiar with point of care ultrasound. (Jacobson et al., 2016) Dry needling is an old therapy that is regaining popularity, and it may be functioning in a similar fashion.

High Volume Saline Injections
An interesting treatment involving injection of high volumes of saline around the affected tendon has shown good promise. It probably works by interrupting the neovascularization. (Boesen, Hansen, Boesen, Malliaras, & Langberg, 2017; Chaudhry, 2017; Morton et al., 2014; Spang, Chen, & Backman, 2016)

Conclusion
Thus, we are in the midst of a paradigm shift in the treatment of tendinopathy, where in some cases, rather than limiting inflammation, we need to increase it in a measured fashion. It is also important to realize that some of the pain related to tendinopathy arises from neovascularization, which requires treatment aimed outside the tendon. This can be done with fairly simple therapies such as exercise, manual therapies, and ultrasound directed injections. Previously common anti-inflammatory therapies have limited utility.

References


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