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Getting tendinopathy treatment (and terminology) right

Tendinopathy, tendinitis, tendinosis, paratenonitis—they are not synonymous. Here you'll find a review of their pathophysiology and best approaches to treatment.

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PRACTICE RECOMMENDATIONS

› *Recommend eccentric exercises to treat patients with tendinosis; research has consistently shown them to be an effective and safe treatment for many types of this disorder.* (A)

› *Use corticosteroid injections with caution for tendinosis; pain relief is typically short lived, and good evidence exists for long-term relapse and worse outcomes including post-injection tendon rupture, especially in the lower extremity.* (A)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

The vast majority of patients with tendon problems are successfully treated nonoperatively. But which treatments should you try (and when), and which are not quite ready for prime time? This review presents the evidence for the treatment options available to you. But first, it's important to get our terminology right.

Tendinitis vs tendinosis vs paratenonitis: Words matter

The term "tendinopathy" encompasses many issues related to tendon pathology including tendinitis, tendinosis, and paratenonitis.[1,2] The clinical syndrome consists of pain, swelling, and functional impairment associated with activities of daily living or athletic performance.[3] Tendinopathy may be acute or chronic, but most cases result from overuse.[1]

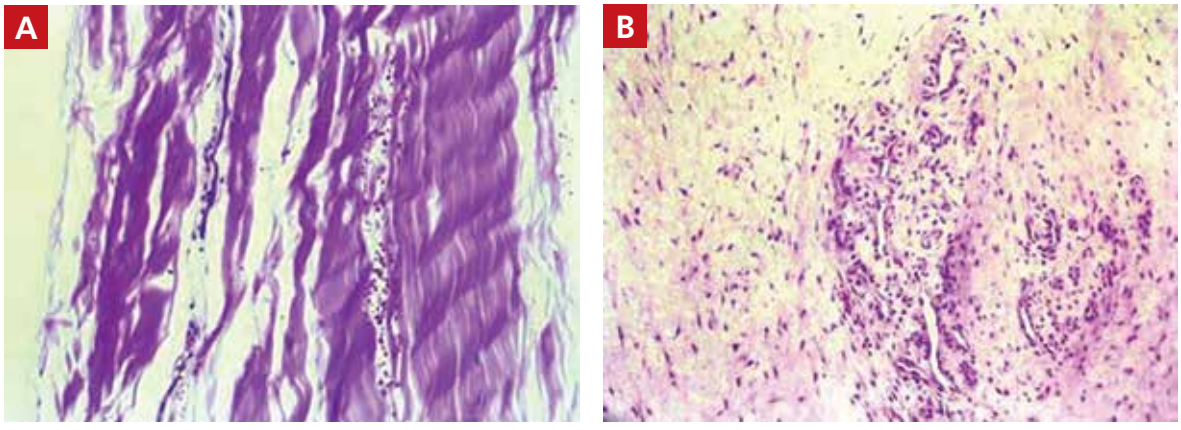
In healthy tendons, the collagen fibers are packed tightly and organized in a linear pattern (**FIGURE 1A**). However, tendons that are chronically overused develop cumulative microtrauma that leads to a degenerative process within the tendon that is slow (typically measured in months) to heal. This is due to the relative lack of vasculature and the slow rate of tissue turnover in tendons.[2,4,5]

Sports and manual labor are the most common causes of tendinopathy, but medical conditions including obesity, high blood pressure, diabetes, and high cholesterol are associated risk factors. Medications, particularly fluoroquinolones and statins, can cause tendon problems, and steroids, particularly those injected intratendinously, have been implicated in tendon rupture.[4,6]

The term "tendinitis" has long been used for all tendon disorders although it is best reserved for acute inflammatory conditions. For most tendon conditions resulting from overuse, the term "tendinosis" is now more widely recognized and preferred.[7,8] Family physicians (FPs) should recognize that ten-

FIGURE 1

Normal tendon vs tendinosis



On histology, the normal tendon is tightly packed with collagen fibers organized in a linear pattern with relatively few cells present (**A**). Tendinosis, on the other hand, has a disorganized pattern with increased cellularity and mucoid ground substance (**B**).

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dinitis and tendinosis differ greatly in pathophysiology and treatment.[3]

Tendinitis: Not as common as you think

Tendinitis is an acute inflammatory condition that accounts for only about 3% of all tendon disorders.[3] Patients presenting with tendinitis usually have acute onset of pain and swelling typically either from a new activity or one to which they are unaccustomed (eg, lateral elbow pain after painting a house) or from an acute injury. Partial tearing of the affected tendon is likely, especially following injury.[2,3]

Tendinosis: A degenerative condition

In contrast to the acute inflammation of tendinitis, tendinosis is a degenerative condition induced by chronic overuse. It is typically encountered in athletes and laborers.[2,5,8,9] Tendinotic tissue is generally regarded as noninflammatory, but recent research supports inflammation playing at least a small role, especially in closely associated tissues such as bursae and the paratenon tissue.[10]

Histologically, tendinosis shows loss of the typical linear collagen fiber organization, increased mucoid ground substance, hypercellularity, and increased growth of nerves and vessels (**FIGURE 1B**).

Tendinosis is not always symptomatic.[5,11] When pain is present, experts have proposed that it is neurogenically derived rather than from local chemical inflammation. This is supported by evidence of increases in the excitatory neurotransmitter glutamate and its receptor N-methyl-D-aspartate in tendinotic tissue with nerve ingrowth. Tendinotic tissue also contains substance P and calcitonin gene-related peptide, neuropeptides that are associated with pain and nociceptive nerve endings.[2,3,6,10]

Patients with tendinosis typically present with an insidious onset of a painful, thickened tendon.[11] The most common tendons affected include the Achilles, the patellar, the supraspinatus, and the common extensor tendon of the lateral elbow.[2] Lower extremity tendinosis is common in athletes, while upper extremity tendinopathies are more often work-related.[3]

Paratenonitis: Inflammation surrounding the tendon

Occasionally, tendinosis may be associated with paratenonitis, which is inflammation of the paratenon (tissue surrounding some tendons).[2,5,10] Paratendinous tissue contains a higher concentration of sensory nerves than the tendon itself and may generate significant discomfort.[10,11]

The clinical presentation of paratenonitis includes a swollen and erythematous

TABLE 1
Types of tendinopathy[2,3,5,6,9-11]

Type	Pathophysiology	Duration	Cause
Tendinitis	Inflammation of a tendon	Acute	Injury or overuse
Paratenonitis	Inflammation of the paratenon surrounding a tendon	Acute	Injury or overuse
Tenosynovitis	Inflammation of the paratenon and the synovial sheath (specific to tendons encased in a synovial sheath)	Acute or chronic	Typically overuse
Tendinosis	Degeneration within a tendon	Chronic	Overuse

tendon.[5] The classic example—de Quervain disease—involves the first dorsal wrist compartment, in which the abductor pollicis longus and extensor pollicis brevis tendons are encased in a synovial sheath. The term *tenosynovitis* is commonly used to indicate inflammation of both the paratenon and synovial sheath (**TABLE 1**[2,3,5,6,9-11]).[5]

Treatment demands time and patience

Treating tendon conditions is challenging for both the patient and the clinician. Improvement takes time and several different treatment strategies may be required for success. Given the large number of available treatment options and the often weak or limited supporting evidence of their efficacy, designing a treatment plan can be difficult. **TABLE 2** summarizes the information detailed below about specific treatment options.

First-line treatments. The vast majority of patients with tendon problems are successfully treated nonoperatively. Reasonable first-line treatments, especially for inflammatory conditions like tendinitis, tenosynovitis, and paratenonitis, include relative rest, activity modification, cryotherapy, and bracing.[12-14]

Nonsteroidal anti-inflammatory drugs (NSAIDs) for pain control are somewhat controversial. At best, they provide pain relief in the short term (7-14 days); at worst, some studies suggest potential detrimental effects to the tendon.[14] If considered, NSAIDs should be used for no longer than 2 weeks. They are ideally reserved for pain control in patients with acute injuries when an inflammatory condition is likely. An alternative for pain control in inflammatory cases is a short course of oral steroids, but the adverse effects of these medications may be challenging for some patients.

Other options. If these more conservative treatments fail, or the patient is experiencing significant and debilitating pain, FPs may consider a corticosteroid injection. If this fails, or the condition is clearly past an inflammatory stage, then physical therapy should be considered. More advanced treatments, such as platelet-rich plasma injections and percutaneous needle tenotomies, are typically reserved for chronic, recalcitrant cases of tendinosis. Various other treatment options are detailed below and can be used on a case-by-case basis. Surgical management should be considered only as a last resort.

Realize that certain barriers may exist to some of these treatments. With extracorporeal shockwave therapy, for example, access to a machine can be challenging, as they are typically only found in major metropolitan areas. Polidocanol, used during sclerotherapy, can be difficult to obtain in the United States. Another challenge is cost. Not all of these procedures are covered by insurance, and they can be expensive when paying out of pocket.

Rehabilitation: Eccentric exercises and deep-friction massage

Studies show that eccentric exercises (EEs)

Reserve use of NSAIDs for pain control in patients with acute injuries when an inflammatory condition is likely.

TABLE 2

Tendinopathy treatment options

Treatment type	Mechanism of action	Administration	Considerations and adverse effects
Rehabilitation (eccentric exercises [**EE**] and deep-friction massage [**DFM**])	**EE**: Reduces vessel and nerve presence in tendons, modulates expression of neuronal substances, and stimulates formation of load-tolerant fibroblasts **DFM**: Induces fibroblast proliferation via cell mediator and growth factor release	Treatment is typically guided by a physical therapist or certified athletic trainer	Both EE and DFM can be painful DFM may cause bruising
Extracorporeal shockwave therapy	Promotes proliferation of healing growth factors (eg, TGF-β1 and IGF-1)	Variations exist in treatment intensity, frequency, duration, timing, number of treatments, and use of local anesthetic	Can be a painful procedure, which is why a local anesthetic is sometimes used
Glyceryl trinitrate patches	Nitric oxide has been shown to enhance collagen synthesis and fibroblast proliferation in animal models	5 mg/24 hr-patch: Cut the patch into quarters, apply over the affected area, then change at 24 hours	Use with caution in cardiac patients or those taking PDE-5 inhibitors May cause rash, headache, and/or dizziness
Corticosteroid injections	The etiology of pain control is unclear, but proposed mechanisms include lysis of peritendinous adhesions, reduced vascularization, and disruption of nociceptors	Injected (blind or image guided) or delivered transcutaneously	Can cause fat atrophy and depigmentation Case reports of tendon rupture following injection Use with caution in patients with uncontrolled diabetes
Platelet-rich plasma (PRP)/whole blood injections	The delivery of growth factors (eg, VEGF, PDGF, and IGF-1) and bioactive mediators induces an anabolic healing response	Autologous blood and PRP are injected directly into the tendinotic tissue, typically with ultrasound guidance	Generally safe May require multiple injections PRP is typically expensive; whole blood is less expensive because there's no manipulation of the blood product

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Platelet-rich plasma injections are typically expensive; whole blood is less expensive because there's no manipulation of the blood product.

help to decrease vascularity and nerve presence in affected tendons, modulate expression of neuronal substances, and may stimulate formation of load-tolerant fibroblasts.[2,3]

For Achilles tendinosis, EE is a well-established treatment supported by multiple randomized controlled trials (RCTs). Improvements in patient satisfaction and pain range from 60% to 90%; evidence suggests greater success in midsubstance vs insertional Achilles tendinosis.[15] The addition of deep-friction massage (DFM), which we'll discuss in a moment, to EE appears to improve outcomes even more than EE alone.[16]

EE is also a beneficial treatment for patellar tendinosis,[3,14] and it appears to benefit rotator cuff tendinosis,[3] but research has

TABLE 2
Tendinopathy treatment options (*cont'd*)

Treatment type	Mechanism of action	Administration	Considerations and adverse effects
Prolotherapy	Involves injecting an irritant to stimulate an inflammatory response leading to the release of growth factors	The irritant is typically hypertonic dextrose (strength 15%-25%) injected into the tendinotic tissue with ultrasound guidance	Generally safe Usual protocols require multiple injections
Sclerotherapy	Sclerosing agents used to destroy the neovascularization and associated sensory nerves	Administration involves injection of a sclerosing agent (eg, polidocanol) under ultrasound guidance with Doppler	Generally safe Requires ultrasound to guide the needle appropriately
Stem cells	It is believed that stem cells differentiate into tenocytes to help produce healthy tendon tissue and stimulate an immune response leading to the production of growth factors and cytokines	Adipose or bone marrow-derived stem cells are expanded and injected (usually with ultrasound guidance) into the pathologic tissue	No high-quality evidence supporting its use Relatively minor adverse effects including local swelling and joint effusion Typically expensive
Percutaneous needle tenotomy	Causes mechanical disruption and bleeding of the tendinotic tissue, releasing growth factors to induce healing	Typically 20-30 needle fenestrations are performed through the entirety of the tendinotic tissue that has been identified on ultrasound	Case reports of post-procedure tendon rupture Prolonged absence from activity is typically recommended after the procedure

shown EE for lateral epicondylosis to be no more effective than stretching alone.[17]

DFM is for treating tendinosis—not inflammatory conditions. Mechanical stimulation of the tissue being massaged releases cell mediators and growth factors that activate fibroblasts. It is typically performed with plastic or metal tools.[16] DFM appears to be a reliable treatment option for the lateral elbow.[18]

Extracorporeal shockwave therapy appears promising; evidence is limited

Research has shown that extracorporeal shockwave therapy (ESWT) promotes the production of TGF-β1 and IGF-1 in rat models,[2] and it is believed to be able to disintegrate calcium deposits and stimulate tissue repair.[14] Research is generally supportive of its effectiveness in treating tendinosis; however, evidence is limited by great variability in studies in terms of treatment intensity, frequency, duration, timing, number of treatments, and use of a local anesthetic.[14] ESWT appears to be useful in augmenting treatment with EE, particularly with regard to the rotator cuff.[19]

A review of 10 RCTs demonstrated the effectiveness of ESWT for tennis elbow.[2] ESWT for greater trochanteric pain syndrome (GTPS, formerly known as trochanteric bursitis) appears to be more effective than corticosteroids and home exercises for outcomes at 4 months and equivalent to home exercises at 15 months.[20] In patellar tendinosis, ESWT has been shown to be an effective treatment, es-

Recommend deep-friction massage for tendinosis—not inflammatory conditions.

pecially under ultrasound guidance.[12] Studies involving the use of ESWT for Achilles tendinosis have had mixed results for midsubstance tendinosis, and more positive results for insertional tendinosis.[15] For a video on how the therapy is administered, see https://www.youtube.com/watch?v=Fq5yqiWByX4.

Glyceryl trinitrate patches: Mixed results

Basic science studies have shown that nitric oxide modulates tendon healing by enhancing fibroblast proliferation and collagen synthesis,[2,14] but that it should be used with caution in cardiac patients and in those who take PDE-5 inhibitors. Common adverse effects include rash, headache, and dizziness.

In clinical studies, glyceryl trinitrate (GTN) patches show mixed results. For the upper extremity, GTN appears to be helpful for pain in the short term when combined with physical therapy, but long-term positive outcomes have been absent.[21] In one Level 1 study for patellar tendinosis comparing GTN patches with EE to a placebo patch with EE, no significant difference was noted at 24 weeks.[22] Benefit for Achilles tendinosis also appears to be lacking.[3,23]

Use glyceryl trinitrate patches with caution in cardiac patients and in those who take PDE-5 inhibitors.

Corticosteroid injections: Mechanism unknown

The mechanism for the beneficial effects of corticosteroid injections (CSIs) for tendinosis remains controversial. Proposed mechanisms include lysis of peritendinous adhesions, disruption of the nociceptors in the region of the injection, and decreased vascularization.[10,15] Given tendinosis is generally regarded as a noninflammatory condition, and the fact that these medications have demonstrated potential negative effects on tendon healing, exercise caution when considering CSIs.[2,24]

Although steroids can effectively reduce pain in the short term, intermediate- and long-term studies generally show no difference or worse outcomes when they are compared to no treatment, placebo, or other treatment modalities. In fact, strong evidence exists for negative effects of steroids on lateral epicondylosis in both the intermediate (6 months) and long (1 year) term.[24] Particular care is required when administering a CSI for medial epicondylosis, as the ulnar nerve is immediately posterior to the medial epicondyle.[25]

In contrast, CSIs appear to be a reliable treatment option for de Quervain disease.[26] Landmark-guided injections for GTPS can improve pain in the short term (< 1 month), but are inferior to either home exercises or ESWT beyond a few months. Thus, CSIs are a reasonable option for pain control in GTPS, but should not be the sole treatment modality.[20]

Studies regarding corticosteroid use for Achilles and patellar tendinosis have had mixed results. Patients can hope for mild improvement in pain at best, and the risk for relapse and tendon rupture is ever present.[27] This is especially concerning given the significant load-bearing of the patellar and Achilles tendons.[14,15] If you are considering a CSI for these purposes, use imaging guidance to ensure the injection is not placed intratendinously.

Platelet-rich plasma and whole blood: Inducing an anabolic healing response

Platelet-rich plasma (PRP) and whole blood injections both aim to deliver autologous growth factors (eg, VEGF, PDGF, and IGF-1) and bioactive mediators to the site of tendinosis to induce an anabolic healing response. PRP therapy differs from whole blood therapy in that it is withdrawn and then concentrated in a centrifuge before being injected. Patients are typically injected under ultrasound guidance. The great variation in PRP preparation, platelet concentration, use of adjunctive treatments, leukocyte concentration, and number and technique of injections makes it difficult to determine the optimal PRP treatment protocol.[10,28,29]

In 1 prospective RCT comparing subacromial PRP injections to CSI for the shoulder, the PRP group had better outcomes at 3 months, but similar outcomes at 6 months. The suggestion was made that PRP therapy could be an alternative treatment for individuals with a contraindication to CSIs.[30]

PRP therapy appears to be an effective treatment option for patellar tendinopathy.[28,31] A Level 1 study comparing dry needle tenotomy and EE to dry needle tenotomy with both PRP therapy and EE found faster

recovery in the PRP group.[32] In another patellar tendon study comparing ESWT to PRP therapy, both were found to be effective, but PRP performed better in terms of pain, function, and satisfaction at 6 and 12 months.[12] For Achilles tendons, however, the evidence is mixed; case series have had generally positive outcomes, but the only double-blind RCT found no benefit.[28,31]

In lateral epicondylosis, the use of autologous whole blood or PRP injections appears to help both pain and function, with several studies failing to demonstrate superiority of 1 modality over the other.[24,25,28,33] This raises the issue of whether PRP therapy is any more effective than whole blood for the treatment of other tendinopathies. Unfortunately, there is a paucity of studies comparing the effectiveness of 1 modality to the other, apart from those for lateral epicondylosis.

Prolotherapy: An option for these 3 conditions

Prolotherapy involves the injection of hypertonic dextrose and local anesthetic, which is believed to lead to an upregulation of inflammatory mediators and growth factors. This treatment usually involves several injections spaced 2 to 6 weeks apart over several months. High-quality studies are not available to clarify the optimal dextrose concentration or number of injections required. The few high-quality studies available support prolotherapy for lateral epicondylosis, rotator cuff tendinopathy, and Osgood Schlatter disease. Lesser-quality studies support its use for refractory pain of the Achilles, hip adductors, and plantar fascia.[24,34]

Sclerotherapy: Not just for veins

As discussed earlier, tendinotic tissue can have neovascularization that is easily detected on Doppler ultrasound. Sensory nerves typically grow alongside the new vessels. Sclerosing agents, such as polidocanol, can be injected with ultrasound guidance into areas of neovascularization, with the intention of causing denervation and pain relief.[15] Neovascularization does not always correlate with pathology, so careful patient selection is necessary.[35]

Studies of sclerotherapy for patellar tendinopathy are generally favorable. One comparing sclerotherapy to arthroscopic debridement showed improvement in pain from both treatments at 6 and 12 months, but the arthroscopy group had less pain, better satisfaction scores, and a faster return to sport.[14] Sclerotherapy is also effective for Achilles tendinosis.[15]

Stem cells: Not at this time

Stem cell use for tendinosis is based on the theory that these cells possess the capability to differentiate into tenocytes to produce new, healthy tendon tissue. Additionally, stem cell injections are believed to create a local immune response, recruiting local growth factors and cytokines to aide in tendon repair. A recent systematic review failed to identify any high-quality studies (Level 4 data at best) supporting the use of stem cells in tendinopathy, and the researchers did not recommend stem cell use outside of clinical trials at this time.[36]

Percutaneous needle tenotomy: Consider it for difficult cases

Percutaneous needle tenotomy is thought to benefit tendinosis by disrupting the tendinotic tissue via needling, while simultaneously causing bleeding and the release of growth factors to aid in healing. Unlike surgical tenotomy, the procedure is typically performed with ultrasound guidance in the office or other ambulatory setting. After local anesthesia is administered, a needle is passed multiple times through the entire region of abnormality noted on ultrasound. Generally, around 20 to 30 needle fenestrations are performed.[37,38]

In one retrospective study evaluating 47 patellar tendons, 81% had excellent or good results.[38] In a retrospective study for lateral epicondylosis, 80% had good to excellent results.[39] JFP

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Exercise caution when considering corticosteroid injections for tendinosis.

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