Dupuytren's Disease: History, Diagnosis, and Treatment

Robert B. Shaw, Jr., M.D.
Alphonsus K. S. Chong, M.D.
Andrew Zhang, M.D.
Vincent R. Hentz, M.D.
James Chang, M.D.

Stanford and Palo Alto, Calif.

Learning Objectives: After studying this article, the participant should be able to: 1. Describe the clinical features of the disease. 2. Describe the pathoanatomical structures in Dupuytren's disease. 3. Outline the various factors associated with Dupuytren's disease. 4. Describe the modalities for surgical and nonsurgical treatment of the condition. 5. Outline recent biomolecular knowledge about the basis of Dupuytren's disease.

Summary: Dupuytren's disease is characterized by nodule formation and contracture of the palmar fascia, resulting in flexion deformity of the fingers and loss of hand function. The authors review the historical background, clinical features, and current therapy of Dupuytren's disease; preview treatment innovations; and present molecular data related to Dupuytren's disease. These new findings may improve screening for Dupuytren's disease and provide a better understanding of the disease's pathogenesis. (*Plast. Reconstr. Surg.* 120: 44e, 2007.)

HISTORICAL BACKGROUND

Plater, in 1614, provided the earliest surgical reference to Dupuytren's disease, attributing the flexion contracture to flexor tendon trauma. Cline dissected a hand with Dupuytren's disease, describing involvement of the palmar fascia and observing that the palmar aponeurosis was thickened.[1] Astley Cooper, Cline's apprentice, attributed thickening of the palmar fascia as the cause of the disease, and suggested that narrow cords could be successfully treated by fasciotomy.[2]

In France, Boyer and Dupuytren both supported the idea that Dupuytren's disease was caused by drying, hardening, and stiffening of the flexor tendons and the overlying skin. It was not until 1831 that Dupuytren dispelled the idea of flexor tendon involvement. During his presentation to the Hôtel-Dieu, Dupuytren described the anatomical features of the disease and related it to the patient's history and clinical presentation. He believed that local trauma was causative and that the disease had a progressive nature.[3,4] Dupuytren described bundles of apo-

neurotic tissue that extended into the involved fingers and proposed that each of these bundles had to be cut during the release while preserving nerves and arteries adjacent to these bundles.

Goyrand added to the growing understanding of Dupuytren's disease with two hand dissections in 1833. He believed that both the flexor tendons and the palmar aponeurosis were normal and that contracture was caused by bands of new fibrous tissue superficial to the aponeurosis. Disease in the thumb also led Goyrand to believe that the palmar aponeurosis was not involved because it was not present in the thumb. He believed that division of these new bands of tissue could correct the flexion deformity and proposed that a longitudinal incision be used.[5]

Sanson, one of Dupuytren's staff, critiqued Goyrand's work in 1834. Although acknowledging that not all cases were limited to the palmar aponeurosis,[6] he believed that the bands described by Goyrand represented proliferation of fibrous tissue from the palmar aponeurosis rather than newly formed tissue. Goyrand remained convinced that metacarpophalangeal joint contracture could not be caused by palmar aponeurosis shortening, reiterating that the disease was caused by bands of abnormal tissue and that the palmar aponeurosis and its extensions played no part in the condition.[7] Although some of Goyrand's observations were accurate, Dupuytren and Sanson were correct in believing that the palmar fascia and aponeurosis were

involved, and that the disease was a proliferation of the tissue that was normally present.

EPIDEMIOLOGY

Dupuytren's disease predominantly affects older men of northern European descent. Disease prevalence varies from 2 to 42 percent, and it is believed to have an autosomal dominant inheritance pattern with variable penetrance.[8] Men are six times more likely than women to present with the condition, and children are rarely affected.[9] Bilateral disease is also more common in men, affecting 59 percent of men versus 43 percent of women.[10] The incidence rises sharply for men in their fifth decade and for women in their sixth decade. By the ninth decade, the prevalence across genders is equal.[11] Disease recurrence is equal in both sexes.

Dupuytren's diathesis is used to describe patients who have a strong predilection for the disease.[12] These patients present at a young age and have a strong family history of the disease. They often have bilateral disease with skin involvement, and are more likely to have ectopic disease.

Dupuytren's disease is uncommon in the black population.[13] Although generally uncommon in Asia, some parts of Japan and Taiwan have a prevalence equal to that in northern Europe. These patients present with a less severe form of the disease, where only nodules are present. The absence of cord formation explains why surgery is not usually needed for these patients.[14]

It has been believed that there may be a relationship between manual labor and onset of the disease.[15] Proponents of this causal relationship believe that trauma to the palmar fascia causes fibril ruptures in the collagen.[16] There is an association between Dupuytren's disease and alcohol abuse, with an increased incidence of disease in alcoholics.[17,18] Epilepsy is also often linked to Dupuytren's disease, with the incidence in epileptics as high as 56 percent.[19]

There are also links to diabetes mellitus and smoking. Dupuytren's disease has been reported to be three times higher in smokers, which may be related to the microvascular changes in the hand that occur with smoking. The higher prevalence in diabetics is often believed to be related to the microangiopathy and increased collagen production that is present.[20] It is interesting that diabetics also have increased rates of flexor tenosynovitis and carpal tunnel syndrome, other common "inflammatory" or "proliferative" processes in the hand. Rheumatoid arthritis is the only condition that has been associated with a lower incidence of Dupuytren's disease.[21]

CLINICAL PRESENTATION

Dupuytren's disease usually occurs bilaterally, with one hand being more involved than the other. The typical findings are the presence of a nodule followed by the formation of a cord.[22] The contracture usually starts in the palm and then progresses distally. The ring finger is most often involved, followed by the small finger, thumb, and middle and index fingers. There may be skin changes such as pitting and dimpling. The palmar skin and underlying tissue thicken, and the subcutaneous fat becomes more fibrotic, leading to the skin becoming more attached to the underlying fascial structures. Skin pits are usually seen in the palm distal to the distal palmar crease. They result from the contraction of the longitudinal fibers of the palmar aponeurosis that insert into the dermis. These skin changes can be the earliest sign of disease.

Nodules, a key diagnostic feature, are elevated, firm soft-tissue masses, commonly fixed to the skin and palmar fascia. Nodules can present in both the palm and digits. Palmar nodules are usually located near the distal palmar crease. These nodules give way to the formation of a cord as disease progresses. The cord blends in with the nodule as it first forms and is also adherent to the skin. As the cord matures, it becomes more prominent and takes on the rigid appearance of a "pseudotendon."

Ectopic disease is most often found on the hand dorsum, where patients present with Garrod's nodes or knuckle pads. Knuckle pads are fibrosing lesions located in the dorsal skin over the proximal interphalangeal joint.[23] They are often related to bilateral disease, with one study showing that 81 percent of patients with knuckle pads had some form of bilateral disease, whereas only 48 percent of patients without knuckle pads had bilateral involvement.[24] The presence of knuckle pads, however, is not an accurate measure of stage or severity of the disease; by themselves, knuckle pads do not cause any contracture deformity. Patients with knuckle pads do, however, have a higher rate of concurrent ectopic disease such as Lederhose disease (plantar fibromatosis) or Peyronie disease (penile fibromatosis). Plantar fibromatosis is characterized by the plantar fascia becoming more fibrotic and rigid, but it rarely results in any symptoms or contracture of the toes.[25] Patients with Peyronie disease

Table 1. Common Diseased Cords in Dupuytren's Disease

Disease Structure	Origins	Clinical Significance
Palmar cords		
Pretendinous cord	Pretendinous band	Most common cord in hand; causes MPJ flexion contracture; does not displace neurovascular bundle
Vertical cord	Uncommon, from diseased vertical fibers of McGrouther or septa of Legueu and Juvara	May cause painful triggering
Palmodigital cords		
Spiral cord	Pretendinous band, spiral band, lateral digital sheet and Grayson's ligament	Displaces the neurovascular bundle palmarly and to the midline, creating a "spiral nerve"
Natatory cord	Distal fibers of natatory ligament	Web space contracture limiting digital abduction
Digital cords		
Central cord	Extension of pretendinous cord in the finger	Does not usually displace the neurovascular bundle
Retrovascular cord	Retrovascular band of Thomine	Causes DIPJ contracture and prevents full correction of PIPJ contracture
Lateral cord	Lateral digital sheet, often associated with pretendinous and natatory cord	Flexion contracture of PIPJ and DIPJ; displaces neurovascular bundle to midline
Abductor digiti minimi cord	Abductor digiti minimi tendon	Flexion contracture of PIPJ
Thumb and first web		
Proximal commissural cord	Proximal commissural ligament	First web contracture
Distal commissural cord	Distal commissural ligament	First web contracture
Thumb pretendinous cord	Pretendinous band	MPJ contracture

MPJ, metacarpophalangeal joint; DIPJ, distal interphalangeal joint; PIPJ, proximal interphalangeal joint.

have fibrosing lesions on the dorsal or ventral surface of the penis.

ANATOMY

In Dupuytren's disease, the normal anatomy of the hand becomes distorted as the normal palmar fascial bands become diseased cords (Table 1).[26] Most cords occur in the palm and cause metacarpophalangeal joint flexion deformity. The pretendinous cord is most frequently seen (Fig. 1). It develops from the pretendinous band and may be continuous with the lateral and central digital cords. This cord may bifurcate, with each distal end leading to an adjacent digit, but does not commonly displace the neurovascular bundle.[27] The vertical and natatory cords are two other palmar cords. The uncommon vertical cord, usually a small cord segment branching off the pretendinous cord, runs between the neurovascular bundle and the flexor tendon sheath. The natatory cord originates from the distal natatory ligament and is found in the second to fourth web spaces.

The palmar fascia is continuous with the digital fascia, explaining why the contracture is transmitted from the palm to the digits. Digital cords are responsible for the proximal interphalangeal joint flexion deformity and usually are on one side of the digit. The most frequent digital cords in order of appearance are the central, spiral, and lateral cords. More than one type of cord can exist in a digit, termed a combination cord.

The central cord is an extension of the pretendinous cord into the finger. It forms along the

Fig. 1. Recurrent Dupuytren's disease. The surgical incisions over the palm, thumb, and small fingers indicate previous surgery. Note the flexion contracture of the metacarpophalangeal and proximal interphalangeal joints.
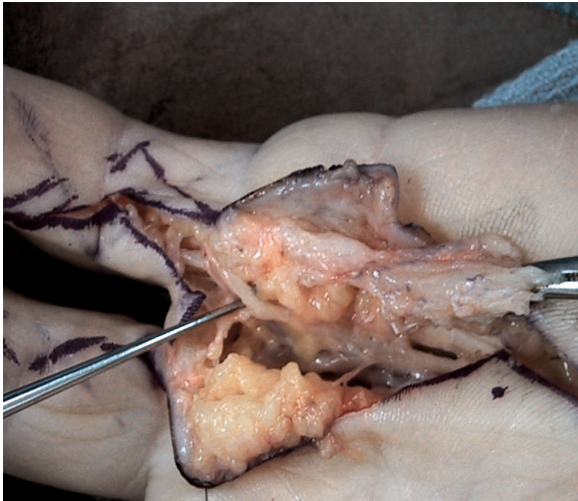
Fig. 2. A spiral band causing volar and midline displacement of the digital nerve as indicated by the instrument on the left side. This anomalous location of the nerve puts it at risk of injury during skin incision and surgical exposure.

Grayson's ligament. The cord begins as a pretendinous cord in the palm and passes deep to the neurovascular bundle just distal to the metacarpophalangeal joint. The cord then runs lateral to the neurovascular bundle as it starts to involve the lateral digital sheet and then runs superficial to the neurovascular bundle as it begins to fuse with Grayson's ligament. As the contracture becomes more severe, the cord straightens and the neurovascular bundle begins to spiral around the cord, which causes it to be displaced toward the midline and closer to the surface of the palm. Because of its superficial displacement, this nerve is now at risk during surgery (Fig. 2). One should expect to see a spiral cord when proximal interphalangeal joint contracture and an interdigital soft-tissue mass are present.[28]

In the small finger, the spiral cord may be located solely in the digit and is known as the abductor digiti minimi cord (Fig. 3). This cord arises from the abductor digiti minimi muscle and runs superficial to the neurovascular bundle, occasionally displacing it. It inserts at the base of the middle phalanx but may also attach to the distal phalanx, causing a distal interphalangeal joint contracture.

midline between the neurovascular bundles, which are rarely displaced, and attaches to the flexor tendon sheath or the periosteum of the middle phalanx. The spiral cord consists of a pretendinous band, a spiral band, the lateral digital sheet, and

The lateral cord is formed from the lateral digital sheet and is often present with the preten-
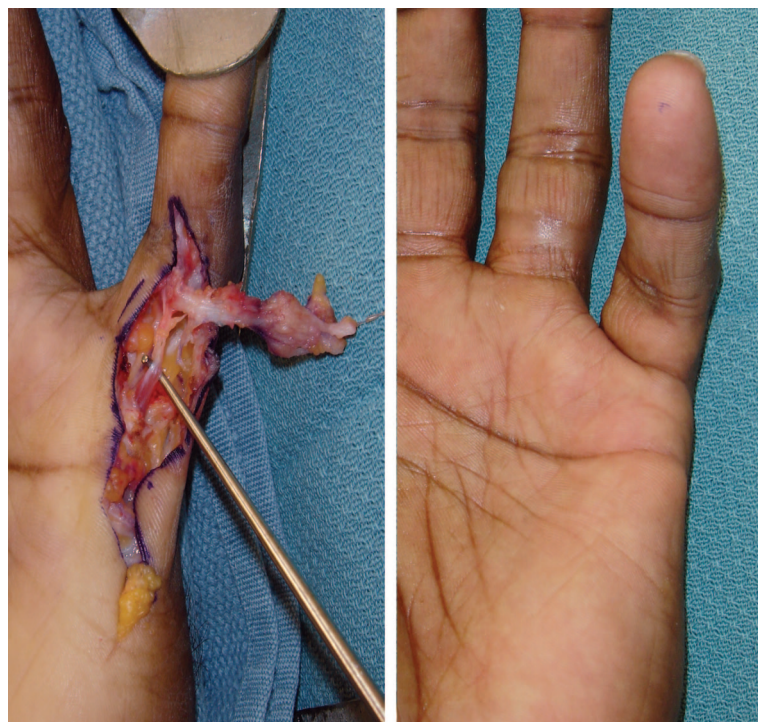

Fig. 3. Partially resected abductor digiti minimi cord arising from its namesake muscle (under hook on the *left*) causing proximal interphalangeal joint contracture (*right*).

dinous cord and natatory cord. It is attached to the skin or tendon sheath through Grayson's ligament, resulting in contracture of the proximal interphalangeal joint and possibly the distal interphalangeal joint, and can cause displacement of the neurovascular bundle toward the midline.

Four different cords can form near the thumb and radial side of the hand.[22] The proximal commissural cord originates from the proximal commissural ligament, and the distal commissural cord is an extension of the distal commissural ligament, with both causing first web contractures. The thumb pretendinous cord is similar to other pretendinous cords and causes metacarpophalangeal contracture. Lastly, the thenar cord is a product of the thickening of the thenar fascia and is associated with the thumb pretendinous cord.

SURGICAL MANAGEMENT

Surgical intervention is usually considered when there is a metacarpophalangeal contracture of at least 30 degrees or any degree of proximal interphalangeal joint contracture. Multiple options exist for skin incisions, including midline longitudinal incisions closed with Z-plasties, multiple Y-V advancement flaps, and Bruner-type zigzag incisions[29] (Figs. 4 and 5). Transverse incisions may also be used, depending on surgeon preference. Although these incisions are usually closed, the wound may also be allowed to heal secondarily with the
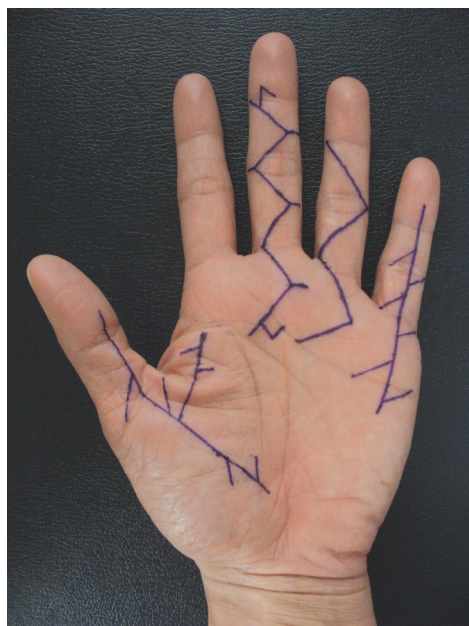
Fig. 4. Some common incisions used for surgical exposure. Note the use of Y-V–plasties for additional skin along the length of the finger and Z-plasties to prevent flexion contractures.

open palm technique of McCash.[30] All of the above incisions should not cross joint creases unless interrupted by Z-plasties.

In recurrent cases, excision of scarred, involved skin may be necessary. The skin is usually removed with the underlying fascia in a dermofasciectomy. Full-thickness skin grafts may be used to replace the removed tissue. This technique was popularized by Hueston, as he often used it to replace a skin shortage, to produce a "firebreak," or to replace dermis that had been infiltrated with myofibroblasts.[31,32]

Four different procedures that address the diseased fascia may be performed: fasciotomy, local fasciectomy, regional fasciectomy, or radical fasciectomy (Table 2). Fasciotomy divides the diseased cords without excision,[33] risking higher recurrence rates. In local fasciectomy, a portion of diseased cord is removed. Because not all of the diseased tissue is removed, the chance of recurrence is also higher.[34] Therefore, both fasciotomy and local fasciectomy are not widely used today.

The most widely used procedure is regional fasciectomy. It is usually carried out through a longitudinal incision.[35] The diseased longitudinal fibers of the palmar fascia are dissected free as far proximally as necessary. The longitudinal cord is then isolated and divided out from the surrounding fascia in a proximal to distal direction. Within the digit, the cord is isolated and followed to its distal attachment and divided.

Radical fasciectomy entails extensive removal of the palmar and digital fascia. The goal is to remove all the longitudinal fibers to the digits. Large skin flaps are necessary to allow access to the entire palm, making flap necrosis more likely. This procedure is not popular, as it has more complications without lower recurrence rates.[36]

The metacarpophalangeal joint contracture is easily corrected because the intrinsic properties of the joint allow it to withstand immobilization in flexion. This is not true for the proximal interphalangeal joint. Prolonged contracture of this joint makes release more difficult, and formal capsuloligamentous release may be necessary. Capsuloligamentous release remains controversial, as it has not shown improved results compared with fasciectomy alone. McFarlane states that this procedure leads to further joint scarring and contracture.[37] It can also lead to scarring, limiting digital flexion. Correction of proximal interphalangeal joint contracture to 30 degrees is often considered satisfactory.
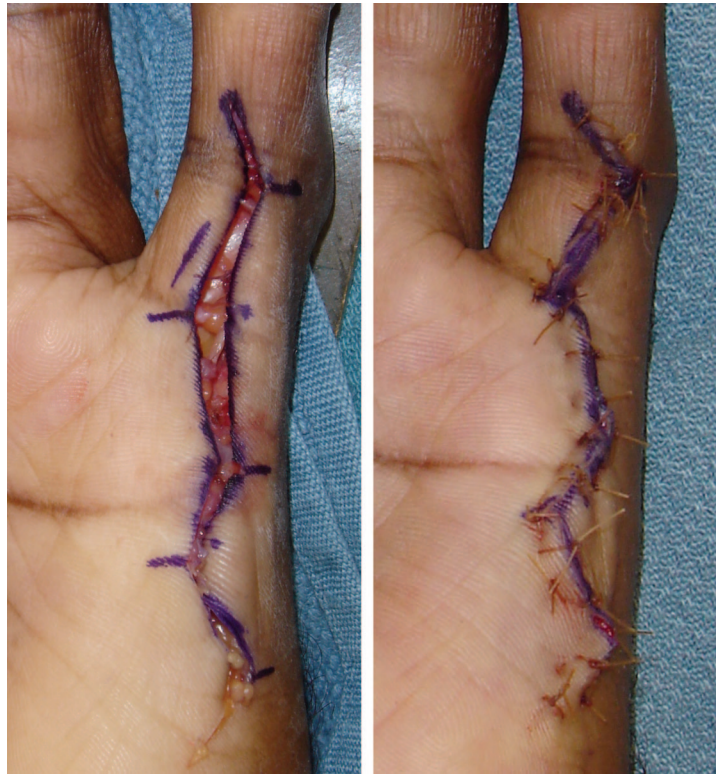
Fig. 5. An example of a Y-V–plasty for the small finger. Note the increased skin along the length of the finger after closure.

Table 2. Surgical Techniques in Dupuytren's Disease

Surgical Technique	Description
Fasciotomy	Division of diseased cords without excision; it can be performed percutaneously
Local fasciectomy	Removal of some diseased tissue
Regional fasciectomy	More extensive dissection and removal of involved tissues
Radical fasciectomy	Removal of all the palmar fascia with extension into the involved fingers; the extensive dissection and skin flaps required increases the risks of complications
Open palm technique (McCash)	Transverse skin incision and division of the aponeurosis, leaving the palm wound open; requires prolonged postoperative splintage
Dermofasciectomy	Removal of the skin and fascia followed by coverage with skin grafts

In the immediate postoperative period, the hand is immobilized with the metacarpophalangeal joints and the proximal interphalangeal joints extended. After several days, active motion is initiated, with a nighttime extension splint to preserve extension. In cases of multiple recur-rences and neurovascular damage or involvement, it might be necessary to consider salvage procedures such as arthrodesis or amputation. The results following surgery for Dupuytren's contracture varies widely in the published literature. This is likely because of differences in definition of recurrence and duration of follow-up rather than true differences in surgical outcome. It is accepted that the recurrence rate increases with time.[38] Between 41 and 54 percent or more of patients will develop some recurrence by 5 years.[39–41] However, recurrence does not equate with need for further treatment. Rodrigo et al. found that only 15 percent of recurrences warranted reoperation.[34]

The rate of complications is high, with McFarlane and Botz reporting them in 17 percent of cases.[42] Complications are more likely to occur in patients who have severe or recurrent disease. These include digital nerve injury, infection, ischemia, hematoma, stiffness, skin loss, and wound-healing problems. Patients may also suffer from pain, stiffness, and vasomotor disorders. Pain syndromes such as Dupuytren's "flare" and complex regional pain syndrome can be present in people with aggressive or early disease. Flare reaction is an inflammatory reac-

tion that can occur 2 to 3 weeks after surgery.[43] It presents as stiffness with pain and edema, and is present more often in women.[44] Complex regional pain syndrome normally occurs after the healing process is complete and has been reported to be present in 5 percent of patients. Again, this disorder is more common in women. It has a similar presentation as flare, but it also involves vasomotor disorders.

BIOMOLECULAR ADVANCEMENTS

Diagnosis and treatment of Dupuytren's disease has not changed significantly in the past three decades. In this era of molecular medicine, new methods to screen and treat this disease may be possible. To initiate this process, three questions are asked: (1) What is the genetic basis of Dupuytren's disease? (2) What occurs on the cellular level in Dupuytren's disease? (3) Can molecular data be used to guide treatment?

What Is the Genetic Basis of Dupuytren's Disease?

DNA microarray technology compares gene expression patterns quantitatively between tissue samples on a genomic scale. Pan et al. first attempted to examine gene expression in Dupuytren's contracture using DNA microarrays.[45] In a separate study, gene expression patterns across 42,000 gene elements were compared among specimens from Dupuytren's diseased cord and control palmar fascia.[46] This showed that in diseased tissue more than 30 unique genes were up-regulated, and six unique genes were down-regulated by fourfold or greater.

This included genes previously shown to be involved in Dupuytren's disease such as fibronectin, tenascin C, transforming growth factor (TGF)-β2, collagen III, collagen IV, and collagen VI. All three isoforms of TGF-β were found to be up-regulated in the cord tissue and paracord fascia compared with normal controls. Increased TGF-β2 expression up to 10- to 20-fold, validated by real-time quantitative polymerase chain reaction analysis, was seen in the cord tissue.

The study also identified novel genes that may be involved in Dupuytren's disease, including candidate genes that may play a master regulatory role in disease pathogenesis. A transcription factor named musculoaponeurotic fibrosarcoma oncogene homolog B, or MafB, was found to be highly expressed in the cord tissue. MafB is a basic domain leucine-zipper (bZIP)–type transcription factor of the Maf family of oncogenes. Overexpression of MafB in chicken embryonic fibroblasts induces the formation of colonies.[48] Immunohistochemical analysis showed nuclear staining of MafB in myofibroblasts residing in clusters in cord tissue. MafB was not expressed in the paracord fascia or normal control.

Not surprisingly, many genes that play important roles in extracellular matrix organization and remodeling were found to be highly expressed in diseased cords, along with genes coding for structural proteins such as collagen V, collagen XIV, and NCAM1. A list of the gene expression changes is given in Table 3.[46–67]

What Occurs on the Cellular Level in Dupuytren's Disease?

Contractile myofibroblasts, which leads to flexion contracture deformity,[68] are involved in all stages of the disease.[69] The early proliferative phase is characterized by nodule formation with high fibrinolytic activity (high levels of plasminogen activator), allowing for the differentiation of fibroblasts into myofibroblasts. Myofibroblasts begin to appear during the proliferative phase and comprise nearly all the cells in the nodules. The involutional stage is marked by nodule thickening and the first signs of joint contracture. In this phase, the myofibroblasts are smaller and align in a similar direction along lines of stress in the tissue. Finally, the residual phase is characterized by further contracture caused by collagen deposition. There are very few myofibroblasts in this phase, and the tissue is fairly hypocellular, with dense type I collagen cords remaining. Overall, with the increase of myofibroblasts, there is also an increase in type III collagen, which is usually absent in adult palmar fascia.[70]

Myofibroblasts appear to be fibroblastic in origin but also have characteristics of smooth muscle cells.[71] One characteristic is the presence of actin microfilaments organized into bundles parallel to the long axis of the cell. The bundles are also continuous with extracellular fibrils of fibronectin along the surface of the myofibroblast that help in forming an attachment site called a fibronexus, the structural mechanism by which the contractile force of the intracellular actin filaments is transmitted to the extracellular tissue.[72] The presence of more crosslinking in the collagen also helps in spreading the contractile force throughout the tissue.

The cause of the myofibroblast proliferation in Dupuytren's disease is unknown. One hypothesis is that narrowing of vessels causes ischemia and the generation of free radicals, which then

Table 3. Summary of Changes in Gene Expression in Dupuytren's Disease

Gene	Remarks
Increased gene expression	
TGF-β	All isoforms are increased; TGF-β has been shown to be important in wound healing and scar formation
Fibronectin	Extracellular protein that binds to cell membrane integrins and extracellular matrix; involved in wound healing
Tenascin C	Cell-substrate adhesion molecule like fibronectin involved in wound healing
Collagens III, IV, V, VI, and XIV	Extracellular matrix components
NCAM1	Neural cell adhesion molecule, a cell surface glycoprotein that plays a role in embryogenesis and contact-mediated interactions between neural cells
FAP	Fibroblast activation protein
ADAM12	Induces actin cytoskeleton and extracellular matrix reorganization during early adipocyte differentiation by regulating β1-integrin function
OSF-2	Involved in extracellular matrix turnover
SPARC	Osteonectin; it may play a role in bone metabolism and extracellular matrix production
Dermatopontin	Small leucine-rich proteoglycan involved in collagen fibrillogenesis
Aggrecan 1	Chondroitin sulfate proteoglycan 1, a large proteoglycan found to protect cartilage collagen from proteolytic cleavage of MMPs
MMP 2, 11	Matrix metalloproteinases degrade extracellular matrix elements and are involved in tissue turnover
Contactin 1	Cell adhesion molecule that interacts with tenascin-C in neurite outgrowth
DSCR1	Down syndrome critical region gene 1, regulates the hypertrophic response to mechanical overload in cardiac myocytes
RAB31	Member of Ras oncogene family; involved in vesicular transport of proteins between all compartments of cell during exocytic and endocytic pathways
TREM1	Triggering receptor that may play a role in exocytosis
RIS1	Marker of Ras-induced senescence suggesting the potential role of Ras oncogene in Dupuytren's disease.
PYCR1	Pyrroline-5-carboxylate reductase 1; may play a role in inducing apoptosis
Decreased gene expression	
PAP2b	Phosphatidic acid phosphatase type 2B; involved in cell-to-cell adhesion in endothelial cells
DDR2	Discoidin domain receptor 2; activated by collagen
Clusterin	Glycoprotein with unclear function at present
Thioredoxin interacting protein	It has been found to reduce melanoma cell metastasis
Ring finger protein 13	Part of the ring finger family of proteins with DNA-binding functions
IGF binding protein 6	Secreted protein that modulate the activities of IGF

damage the surrounding tissue and cause fibroblast proliferation.[73] This leads to the formation of myofibroblasts and collagen, causing further ischemia and starting a vicious cycle.

Myofibroblast proliferation can also be stimulated by various growth factors and cytokines. Platelet-derived growth factor (PDGF), TGF, basic fibroblastic growth factor, interleukin-1α and interleukin-1β have all been shown to inhibit myofibroblast expression. TGF-β2 is a potent stimulator for proliferation in both the proliferative and involutional stages of the disease.[74] It has also been shown that mechanical stress can up-regulate myofibroblast differentiation.[75]

Because actin is unique to the myofibroblast, modulating its expression might control the progression of Dupuytren's disease. A recent study showed that 40 percent of the cells expressed smooth muscle actin in Dupuytren's hypercellular nodules.[76] This actin appears during the proliferative phase and seems to correspond with the development of the contracture, as it would cause the cells to "crimp." TGF-β was shown to increase actin expression, whereas platelet-derived growth factor-BB decreased it.

Androgen receptors are expressed in the Dupuytren's nodules.[77] Cells from Dupuytren's patients stimulated with 5α-dihydrotestosterone showed higher rates of proliferation than controls,[78] suggesting that androgens may be important for myofibroblast proliferation in Dupuytren's disease.

Can Molecular Data Be Used to Guide Treatment?

An effective nonsurgical treatment in early Dupuytren's disease would obviate surgical risks. Modulating actin and androgen receptor expression in

the diseased tissue may prevent progression of the disease. Further research into these two growth factors could also provide new targets for treatment. Although gene expression analysis alone cannot provide an integrated molecular understanding of disease pathogenesis, it provides a global gene expression profile of the diseased cords and helps identify target genes for further studies.

One of the most encouraging results in the nonoperative management of Dupuytren's disease has been with collagenase enzymatic fasciotomy. Cords in Dupuytren's disease are composed of type 1 collagen, making them susceptible to collagenase. However, tendon and normal palmar fascia, which lie in close proximity, also contain collagen. This makes it necessary for the treatment to be localized in the cord or diseased tissue alone.

Clostridial collagenase injected into cords has been shown to decrease their elasticity by 93 percent.[79] A phase II clinical study showed that 10,000 units of collagenase injected into the cord results in a reduction of the joint contracture to within 0 to 5 degrees of normal in 90 percent of patients.[80] Ultrasonographic imaging was used to guide the injection into the cord. After the injection, the hand was manipulated, often rupturing the cord. Patients performed daily exercises and were instructed to wear an extension splint at night for 4 months.

In this study, the mean flexion contracture was 44 degrees, suggesting that collagenase therapy would be effective for mild and moderate disease. Its role in more severe disease is not known. Complications described in the study include short-term pain, ecchymosis, edema, and occasional elbow and/or axillary lymphadenopathy.

These early results are promising and, currently, U.S. Food and Drug Administration–approved phase III studies are being prepared. Collagenase is not a cure and long-term recurrence rates have not been determined. However, repeat injections could be used to treat recurrences. Currently, surgery remains the mainstay of treatment. Progress made in the molecular aspects of this disease will open new research avenues, ultimately leading to new forms of treatment for those with this condition.

James Chang, M.D.
Division of Plastic and Reconstructive Surgery
Stanford University Medical Center
770 Welch Road, 4th Floor
Stanford, Calif. 94305
changhand@aol.com

DISCLOSURE
The authors have no financial interests to disclose.

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