# Dupuytren's Disease: Review of the Current Literature

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**Abstract:** Dupuytren's disease is one of the most common condition seen by hand surgeons. It is not only prevalent but can also be a most debilitating condition resulting in significant loss of function of the fingers involved. The cause of this disease, however still remains largely unknown although some recent evidence suggests a stem cell etiology. This review article summarizes the current known knowledge of Dupuytren's as well as the clinical findings, investigations and treatments available.

**Keywords:** Contracture, Dupuytren's disease, Dupuytren's nodules, fasciectomy, hand.

Dupuytren's disease is a fibroproliferative condition of the palmar fascia and results in thickening and shortening of the normal fibrous bands in the hand and fingers. Although benign, the disease can cause disabling, progressive digital contractures.

The earliest published description of the disorder was in 1614 by Felix Platter [1], but it was Guillian Dupuytren who presented a meticulous anatomic and pathological study in 1831[2]. What was unique about Dupuytren's description was that he emphasized the clinical course of the disease and described the procedure of fasciotomy for its treatment.

## EPIDEMIOLOGY

The reported prevalence of Dupuytren's disease varies from 2% to 42%. This wide variety is influenced mainly by ethnicity, gender and age [3, 4]. The highest prevalence is observed in Scandinavia, Great Britain, Ireland, Australia and North American populations [5-7]. Men are more commonly affected by the disease with a male: female ratio ranging between 3.5:1 and 9:1 [8, 9]. The incidence rises sharply after the fourth and fifth decade, with men and women being affected by the same frequency after the age of 80 years [3].The incidence of Dupuytren's disease increases with concurrent disorders and behavioral factors such as diabetes, alcoholism, smoking, HIV infection and hyperlipideamia [10-12]. The effect of convulsive disorders on the incidence of the disease is yet to be established [13, 14].

## ETIOLOGY

The cause of Dupuytren's disease remains unclear despite the advanced understanding of the disease in the last

decade. Dupuytren suggested that the disease was caused by local trauma [15]. Although some studies have supported this relationship others have failed to confirm this [16]. Some have implicated a genetic predisposition to the disease [4, 17-19]. An autosomal dominant inheritance pattern with variable penetrance has been suggested [4] as well as more complex traits [19]. The correlation between Dupuytren's disease and occupation, mainly vibration and manual work, is still debatable [20-22]. Other etiologic mechanisms that have been implicated include free radicals [23], autoimmune [24] and neoplasia [25].

## PATHOPHYSIOLOGY

The pathological nodules and cords in Dupuytren's disease are the result of a fibroproliferative disorder of the palmar aponeurosis. Hystologically the disease progresses through three different phases namely; Proliferative, involution and residual phases [25].

The proliferative stage is characterized by fascial fibroplasia, nodule formation and proliferation of fibroblasts. It is believed that uncontrolled fibroblast proliferation is responsible for the nodule formation. Under the influence of local mediators such as transforming growth factor - TGF-$\beta$1, and the recently suggested periostin [26] the cells can be induced to transform to myofibroblasts [27]. The control of myofibroblast transformation within the Dupuytren tissue shares common features with that observed in the process of granulation and wound healing [28].

During the subsequent involution phase rearrangement of the cells along the stress lines of the tissue occurs. Macroscopically cords begin to develop. The myofibroblasts are the predominant cells in this phase. They have morphological features of fibroblasts and smooth muscle cells [29] and have the ability of synthesizing collagen and alpha-smooth muscle actin which plays a role in contraction [29, 30]. The excessive collagen production leads to nodules formation, while the diseased cords result from the increased

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fraction of collagen type III [31, 32], and the resultant deposits. The abnormal collagen cross-linkage and the continuous contraction of the myofibroblasts result in the subsequent contractures.

In the residual phase the nodules regress leaving thick cords and a relatively acellular residual tissue. The cords become visible, and the contractures severe.

Other growth factors have been found with increased expression within the diseased tissue, these include fibroblast growth factor and platelet-driven growth factor [33]. In their recent study Forsman *et al.* demonstrated a decrease in expressed myoglobin, and an increase in tyrosine kinase – like orphan receptor. The later protein is associated with other diseases of the hand [34]. Metalloproteinase act to mediate regulation of the tensile strength of the abnormal fibroblasts in Dupuytren's disease, this activity seems to have an additional role in the development of Dupuytren's changes [35, 36].

## PATHOANATOMY

Dupuytren's disease affects the palmar fascial complex, the disease cords originate from the normal fascial bands within the palm and digits [37]. Palmar cords result in metacarpophalangeal contractures whereas digital cords result in proximal interphalangeal contractures.

**Palmar cords** are the most common cords and include:

**Peritendinous cords** are the most common among the palmar cords. They originate from the peritendinous fascial band and can be continuous with the digital cords [38] or may bifurcate distally to different digits. These cords usually do not displace the neurovascular bundle [39]. They arise from the peritendinous bands, which are the extension of the longitudinal fibers of the central aponeurosis in the digits II-IV and of the radial and ulnar aponeurosis in the thumb and small finger respectively. Each peritendinous band bifurcates distally and forms three layers: superficial, middle and deep [39]. The middle layer passes to the digit as the spiral band

**Natatory cords** originate from the natatory ligaments and cause contractures of the second through to the fourth web space. These contractures result in constriction of fingers abduction. The distal natatory ligaments are found in the second to fourth web space at the palmar digital junction and acts to connect the adjacent web skin [40].

**Vertical cords** arise from the vertical fibers. These fibers include small superficial fibers that connect the superficial palmar aponeurosis to the skin, known as Grapow fibers [36], and the septa of Legueu and Juvara, Vertical bands are relatively uncommon.

**Digital cords**: Are responsible for the contractures in the interphalangeal joints.

**Central cords** are the most common among the digital cords. They lie between the neurovascular bundles and continue the Peritendonious cord into the digit. Distally the central cord is attached to the flexor tendon and the periosteum of the middle phalanx. Neurovascular displacement due to a central cord is rare.

**The spiral cord** is the result of pathological blending of the peritendinous band, spiral band, lateral digital band and the Grayson's ligament [41]. Distal to the bifurcation of the peritendinous bands the fibers of the middle layer on each side form the spiral band [42]. They run dorsal to the neurovascular bundles and blends distally with lateral digital band fibers. Grayson´s ligaments are composed of the fibers passing volarly to the neurovascular bundle and attach the lateral digital band to the joint capsule, tendon sheath and the periosteum. The course of the spiral cord around the neurovascular bundle causes multidirectional displacement and thus makes the bundle susceptible to surgical injury [36, 43]. The spiral cord usually causes a severe proximal interphalangeal joint contracture.

**The lateral digital cord** is the result of pathological changes in the lateral digital sheet. The cord causes a proximal interphalangeal contracture and may involve the distal interphalangeal joint as well through Grayson's ligament. The lateral cords may cause a medial displacement of the neurovascular bundle.

Within the digits, duplication's disease usually does not involve the Cleland ligament, the oblique retinacular ligaments, and other deeper fascial layers [44, 45]

**Ulnar cords:** The ulnar border of the palm is a common site of involvement in Dupuytren's disease. The abductor digiti minimi cord arises from the abductor digiti mini muscle or tendon and inserts in the base of the middle phalanx. It runs in the ulnar side of the proximal phalanx and superficial to neurovascular bundle. This cord is not well defined and its origin and course varies frequently. It may inserts distally in the distal phalanx causing a distal interphalangeal contracture.

**Radial cords:** The radial aponeurosis is composed of the two commissural ligaments, the extension of the central palmar aponeurosis known as the thenar fascia and the peritendinous band of the thumb [40]. The distal commissural cord is the radial equivalent of the natatory cord in the first web space. It arises from the distal commissural ligament and is responsible for the first abduction contracture.

**The proximal commissural cord** results from a diseased proximal commissural ligament. The ligament is the radial extension of the superficial transverse fibers of the palmar aponeurosis.

**The thenar cord** is a result of thickening of the thenar fascia. It inserts in the radial aspect of the first metacarpophalngeal joint.

## CLINICAL PRESENTATION

A detailed patient history and a careful physical examination are mandatory and sufficient for making the diagnosis without the need of additional studies [46]. The small and the ring fingers are most commonly affected in the disease [3] with bilateral involvement in the majority of the cases. Palmar skin symptoms occur early in the disease course and include pitting thickening, tenderness and dumpling of the palmar skin. Skin pitting is a result of the involvement and retraction of the vertical Grapow bands. Typically the patient presents with slowly progressive skin symptoms of the palmar surface or, less frequently, of the digits. Palmar nodules, or cords maybe present and the patient may describe a reduced range of motion in the digits.

Dupuytren's nodules are the result of fibroblast proliferation and excessive collagen production and arise from the superficial bands of the palmodigital fascia. The nodules which are fixed to the skin and the deep fascia are firm and may be tender. They are pathognomonic [36, 49] and may appear in the palm or digits. Yet soft tissue tumors of the palm and digits may be confused with Dupuytren's disease [47] and must be excluded from the diagnosis, especially in younger patients and those without known risk factors. Typically the nodules are replaced by the disease cords [48] following a spontaneous regression.

The cords blend with nodules initially and attach the overlying skin by diseased vertical fascial bands [49]. They develop usually distal to nodule in the palmar, palmodigital or digital area. Contractions of the cords, over the course of months to several years, leads eventually to fixed contracture of the metacarpophalngeal joint or the interphalangeal joints. In addition to progressive reduction of the range of motion, nerve compression and vascular displacement may occur as a result of the increasing severity of these contractures.

A simple grading system to assess the involvement of Dupuytren's disease and to monitor progression was described by Tubiana *et al.* in 1968 and although having multiple modifications proposed over the years still remains a simple clinical grading system to use as shown in Table **1** [50]. In this grading system the total flexion deformity of each finger is documented and scored between 0-4 as the table below shows. The addition of a P for Palmar and D for Digit describes where the deformity has mainly arisen from and assists in surgical planning.

**Table 1.    Grading System for Dupuytren's Disease [50]**

| N | Palmar Nodule without Presence of Contracture |
|---|---|
| 0 | No lesion |
| 1 | TFD between 0° and 45° |
| 2 | TFD between 45° and 90° |
| 3 | TFD between 90° and 135° |
| 4 | TFD greater than 135° |

Dupuytren's diathesis was first described by Heuston and implicates more aggressive expression of the disease in patient with certain risk factors [51]. This is an important concept to consider as managing a patients expectations and long term prognosis has a significant impact on the morbidity of the disease. Risk factors that are considered to predict a more aggressive course and higher recurrence rate after surgery include; white race, early age of onset – younger than 40 years, strong family history, bilateral involvement and ectopic manifestation. Ectopic manifestations are most commonly encountered on the dorsum of the hand and includes knuckle pads and Garrods nodes located at the proximal interphalangeal joints [52]. Knuckle pads are present in 44-54% of the patients and most commonly affect the second finger [47, 48]. The prevalence of other ectopic manifestations is higher in the presence of knuckle pads [53]. These ectopic manifestations include plantar fibromatosis which is seen in 6-31% of the patients

[48]. The condition known as Lederhose disease is usually asymptomatic and unlike to cause contracture [54]. Penile fibromatosis or Peyronie disease is caused by the development of fibrous plaques within the penile connective tissue and results in pain and deformity of the penis. The condition is encountered in 2-8% of Dupuytren cases [48, 55].

## NONOPERATIVE MANAGEMENT

Several agents and modalities have been suggested for the treatment of Dupuytren's contracture. Vitamin E, gamma-interferon, dimethylsulfoxide and splinting, have been shown to be ineffective [56]. Local steroids injection has also been performed with limited success [57]. Radiotherapy has been shown to stabilize progression of the disease in several studies, and might be used in the early stages to prevent progression [58]. In their *in vitro* study, Rayan *et al.* found that Verapmil and Nifidipine inhibits myofibroblast contraction, and thus may be useful in the early stages of the disease [28]. The use of 5-Fluorouracil has been found, *in vitro*, to cause a dose-dependent selective and specific decrease in collagen production by inhibition of fibroblast proliferation and myofibroblast differentiation [59]. The authors concluded that the clinical implication is that 5-fluorouracil could possibly reduce the recurrence of Dupuytren's disease in the hand.

One of the newest ideas for nonoperative treatments is with the use of an enzymatic fasciotomy by Clostridium histolyticum collegenase injection. This was approved by the US Food and Drug Administration (FDA) in February 2010. In a phase III trial conducted by Badalamente *et al*, collegenase injection was shown to be safe and effective, with a low recurrence rate. Adverse effects included pain at the injection site, minimal hematoma and swelling [60]. Recently Hurst *et al.* reported the use of Clostridium histolyticum collegenase injection for the treatment of patients with contracture of at least 20º in a randomized controlled double blind study [61]. A significant improvement in the contractures and the range of movement was shown with more than 90% correction in the MCP joint, 66% correction of the PIP joint, and low recurrence rates. The results of these studies are very promising and may lead toward a significant change in our approach to Dupuytren's disease in favor of nonoperative treatment.

## SURGICAL TREATMENT

Despite the advanced understanding of the pathogenesis, and the recently reported promising results of non-operative treatment modalities, surgical intervention remains the therapy of choice for advanced stages of Dupuytren's contracture.

Generally nodules and cords do not cause pain or functional impairment, therefore surgical treatment is not indicated if a contracture is not present. The presence of a cord accompanied by a metacarpophalngeal flexion contracture of more than 30º, or a proximal interphalangeal joint contracture of any degree is accepted indications for surgical intervention [49, 62]. Another indication for surgery is a finger with a neurovascular deficit.

The results of surgery for contracture of the metacarpophalngeal joints are better than those observed in

correction of the proximal interphalangeal joints [63]. As a general role the incisions may be primary closed or left open for secondary healing. Both techniques are reported with good results [64]. Full thickness grafts and rotational flaps may also be used when primary closure is not possible.

**Fasciotomy:** Limited open fasciotomy or percutaneous needle fasciotomy may be performed. In both procedures the fascia is divided without excision. Fasciotomy is the least extensive procedure among those used for the treatment of Dupuytren's disease. Rodrigo *et al.* reported that 43% of patient underwent fasciotomy required repeated surgery [65]. In a more recent study repeated surgery was required in 34% of the cases [66]. The high recurrence rate has resulted in this procedure being limited to the use in elderly debilitated patients in whom more extensive procedures are contraindicated [66, 67], however the temporary relief that can be achieved by a percutaneous release within an outpatient setting cannot be ignored. Neurovascular and flexor tendon injury are the main complications of the procedure.

**Selective fasciectomy:** In this procedure the grossly involved fascia is excised. As the disease extend beyond the limits of the macroscopically involved tissue, all diseased tissue may not be removed. However, good results and a low recurrence rate were reported [68]. Selective fasciectomy is a limited procedure with low complication rates and acceptable results; therefore, selective fasciectomy is very common procedure used for the treatment of Dupuytren's disease

**Radical fasciectomy:** This procedure was described by McIndoe and Beare [69], and included complete removal of the palmar and digits fascia. It was originally performed by transverse palmar incision with the addition of digital z plasties when necessary. Although satisfactory results were reported by McIndoe, later studies have demonstrated similar functional outcome [69] and recurrence rate [66] compared with selective fasciectomy [68, 70]. Radical fasciectomy is not commonly performed, because of the increased morbidity and complication rates. Common complications include hematoma, joint stiffness, and delayed healing.

**Segmental aponeurectomy:** Entails partial removal of one or more segments of diseased fascia through multiple small incisions. Small curved insertions are located over the cord and planned so that they can enable nodule excision. The goal is to create a discontinuity in the retracted aponeurotic band without wide dissection of the fascia itself, and thus eliminate the tension in the retracted cord Good results of the procedure with acceptable recurrence rate were reported [70].

**Dermofasciectomy**: The risk of recurrence following fasciectomy was significantly reduced when excision of the skin overlying the cord and skin grafting was added [71]. Hueston suggested that dermis and the underlying layers provide a source for the disease recurrence [72]. In dermofasciectomy the diseased fascia and the overlying skin are resected. Early studies reported prevention of recurrence especially when the procedure was accompanied by the use of full thickness grafts [73]. However, more recent studies have reported a low rate of recurrence [74].

Dermofasciectomy combined with skin grafting is usually used for the treatment of recurrent disease.

**Amputation**: In the setting of Dupuytren's disease amputation is carried out at the level of the proximal interphalangeal joint. It is indicated in cases of severe uncorrectable contracture or neurovascular damage. In a recent report finger amputation due to Dupuytren's disease was found to be the predominant reason for elective finger amputation in adults. Among the procedures performed for the treatment of Dupuytren's disease 2% were elective amputations [75].

As a general rule following surgical treatment, the hand is dressed and splinted with the metacarpophalngeal joints in a position of function (45-70° flexion) and the proximal interphalangeal joints extended [74, 76]. Physiotherapy is commenced immediately to avoid stiffness.

## THE ROLE OF STEM CELLS

The source of abnormal cells leading to Dupuytren's disease formation remains underexplored. In addition to fascia, palmar skin and fat-derived cells may be a potential source of cells causing Dupuytren's disease. A study aimed to profile haematopoietic and mesenchymal stem cells in different Dupuytren's disease tissue components compared with tissue removed at carpal tunnel surgery as control [77]. Fluorescence-activated cell sorting (FACS) and quantitative real-time polymerase chain reaction (QRT-PCR) analysis identified the highest RNA expression and number of cells positive for adipocyte stem cell markers (CD13 and CD29) in the Dupuytren's disease nodule. CD34 RNA was overexpressed, and a higher percentage of these cells were present in Dupuytren's disease skin compared with carpal tunnel skin. Each structural component of Dupuytren's disease had distinct stem cell populations. These findings support the hypothesis that Dupuytren's disease may result from mesenchymal progenitor cell expansion.

## COMPLICATIONS

Intraoperative and postoperative complications of the corrective surgical procedures are common. The reported rate of complications for surgical treatment of Dupuytren's disease ranges from 6% to 46%. Greater initial deformity and more severe disease were found to increase the complication rate [63, 78]. Recurrence, one of the most common and frustrating complication, occurs in 2-60% of cases [63, 74]. This wide variety is explained by the different definition of recurrence used by different authors. As noticed previously, dermofaciectomy seems to result in lower rates of recurrence. The altered anatomy which includes displacement of the neurovascular bundle and the need of dissecting it along the cord increases the risk for neurovascular injury. However this risk may be reduced by applying a meticulous technique. Denkler reviewed the literature pertaining to surgical complications in Dupuytren's disease and noted a major complication rate of 15.7% with injury to the digital nerve occurring in 3.4% of cases and vascular damage during fasciectomy occurring in 2% of cases [79]. Infection is a common wound complication in fasciectomy affecting 3.9% of patients. The presence of a hematoma correlate with higher infection rates, efforts therefore should be made to achieve an adequate

homeostasis. Another wound complication includes flap necrosis and graft failure. Complex regional pain syndrome is a serious and common complication affecting 4.5% of cases following fasciectomy [79] and is far more common in women. It should be noted that the rate of complications dramatically rose in those who underwent further surgery for recurrent contractures.

## SUMMARY

Dupuytren disease is a disabling disorder of the hand of unknown cause. In the last decade several molecular mechanisms have been identified which play a role in the disease pathogenesis. Currently surgical treatment is the most widely offered solution to Dupuytren's as it offers a functional improvement for most of the patients. However, it results in high rates of complications and recurrences. Comprehensive understanding of the complex anatomical nature of the disease is crucial for applying appropriate surgical treatment. Enzymatic fasciotomy using Clostridium histolyticum collegenase is a new local treatment modality with an excellent short term result. Further studies are needed for the evaluation of the long term result, complications and recurrence rate, as well as studies to better ascertain the etiology and determine the role of stem cell therapy.

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## CONFLICT OF INTEREST

None declared.

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