Dupuytrens contracture: Current understanding of the condition and its management

RG Deshmukh\textsuperscript{1}, E Battaloglu\textsuperscript{1}

Abstract

Introduction

This review describes the condition known as Dupuytren’s Contracture, from the historical beginnings leading to its eponymous title, through the most current understanding of the pathophysiology, the clinical aspects of disease recognition, to the latest non-surgical and surgical options used in treatment.

Conclusion

Dupuytren’s disease is a fascinating condition with a variable course and prognosis. Treatment to date has been mainly surgical, though in future non-surgical treatment are set to become increasingly more common and clinically important.

Knowledge of the complex anatomy of the hand is vital in ensuring precise and effective surgical treatment. The relationship of pathological contractures with the neurovascular bundles and flexor tendons requires meticulous procedural skill, even when utilising non-surgical treatments. Limitations of treatment, especially in severe disease, should be recognised, thoroughly explained to patients and evaluated when implementing medical services. Dupuytren’s disease remains a true medical conundrum.

Introduction

Dupuytren’s Disease, a condition characterized by flexion contracture within the joints of the fingers and hands, is a benign fibroproliferative progressive genetic disorder caused by the formation and deposition of abnormal collagen. The condition can also occur in the feet, but most commonly occurs in the ring and little fingers. In the early stage of the condition, nodules of Dupuytren’s tissue form in association with the palmar aponeurosis. These may progress and merge into cords within the fingers or palm. These cords shorten due to the action of myofibroblastic cells within them and restrict extension of the finger, thus resulting in a functional restriction in dexterous tasks. If untreated, although without a predictable rate of progression, the tendency is for worsening of the contractures.

Contractures often span several adjacent joints. For affected joints, if bending one joint allows the adjacent joint to be fully straightened and vice versa, the contracture is referred to as a "composite contracture". If an affected joint cannot be fully straightened in any hand position, the result is called a “fixed contracture”. Despite the majority experiencing a slow rate of onset and progression, in some there can be a rapid deterioration, often termed “Dupuytren’s diathesis”\textsuperscript{1}. Factors associated with Dupuytren’s diathesis include family history, bilateral disease, ectopic lesions, male sex, and an age of less than fifty years at the time of onset. Certain diathesis features in the hand are Garrod knuckle pads, over the dorsal surface of the proximal inter-phalangeal joints, involvement of the radial side of the hands and bilateral hand involvement\textsuperscript{2}.

Extra-palmar locations may be involved including the planter aspect of the foot in Ledderhose Disease or penile fibrosis in Peyronie Disease. The aim of this review was to discuss the current understanding and management of Dupuytren’s contracture.

History

Chronic contracture of the fingers has been depicted in early works back to the medieval times, particularly associated with the Vikings and Celts. Felix Plater, a Swiss physician, described flexion contracture of the fingers in his work, ‘Observationum in Hominis Affectibus’ of 1614\textsuperscript{3}.

Henry Cline, an English surgeon, recognised the affliction in manual labourers in 1787, building from the knowledge of John Hunter, the famous Scottish surgeon\textsuperscript{4,5}. Astley Cooper, a fellow English surgeon in 1822, wrote a detailed description of the contracture of the palmar aponeurosis, in his book ‘A Treatise on Dislocations and Fractures of the Joint’\textsuperscript{6}.

However, the eponymous title of the condition is bore by Guillaume Dupuytren. Dupuytren was a French military surgeon and anatomist, who is credited with giving a lecture in December 1831, at the Hotel-Dieu in Paris regarding the condition\textsuperscript{7}. His French publication in 1832 went on to be translated in to English for print in the Lancet in 1834 entitled ‘Permanent Retraction of the Fingers, Produced by Affiliation of the Palmer Fascia’\textsuperscript{8}. Dupuytren advocated the theory of the condition being as a result of pathophysiology of the palmer aponeurosis\textsuperscript{9}. However, during his later years and following Dupuytren’s death in 1835, many questioned this theory.

Jean-Gaspard Blaise Goyrand, another French surgeon refuted the condition being an isolated affliction of the palmer fascia. He implicated the skin and tendons, basing theory from severe cases, especially involving all the fingers and thumb.

\*Corresponding author
Email: Rajiv.Deshmukh@ulh.nhs.uk

\textsuperscript{1} Pilgrim Hospital Boston, United Lincolnshire Hospitals, United Kingdom

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Alfred Velpeau, a fellow French anatomist and surgeon, did write a more comprehensive and accurate overview of the condition in 1833, however this went mostly ignored. Goyrand is credited with the recognition of the familial nature of the condition and not as a result of a traumatic aetiology.

Epidemiology
Dupuytren’s contracture is a common condition, with prevalence rates of 3 – 5 % in the global population, but this does range between 0.2% to greater than 50% depending upon age and ethnic group.

Genetic susceptibility is a well-recognised aetiological factor. This is supported by numerous epidemiological observations, in particular the very high prevalence of the condition amongst those people of Northern European and Scandinavian origin. However, Dupuytren’s contracture is only rarely seen in African and Asian populations.

In the UK population, prevalence ranges at 10% for males over 55 years old, rising to 15% in males over 70 years old. Moreover, the disease is found to be almost three times higher in individuals with an affected sibling than in the general population. The pattern of inheritance is suggested to be autosomal dominant with variable penetrance.

Men typically present earlier than women, by some 10 years, and men commonly have a more severe disease.

A number of gene alterations, leading to variations in collagen regulation, have been implicated, including genes such as fibronectin, transforming growth factor (TGF-β2), tenasin, collagen III, IV and VI. Mitochondrial defects may also form an underlying pathogenesis for Dupuytren’s Disease. Observations from twin and family studies, looking at trends of Dupuytren’s diathesis in particular, have also supported a strong genetic basis.

Associations
Many studies have examined the link between occupational trauma and Dupuytren’s Disease, yet no conclusive evidence has been forthcoming to demonstrate this. A history of manual labour has been shown to correlate with a worse long term prognosis however. There is still controversy regarding the link with vibration and repetitive trauma, which have been shown in certain studies to result in up to a 5-fold increased incidence of Dupuytren’s disease.

Smoking and alcohol are shown to be independent risk factors for Dupuytren’s disease. Smoking is demonstrated to carry a threefold increased risk, which may be related to the microvascular changes. Alcohol has been shown to cause up to a fourfold increase in the rate of disease development. Chronic liver disease is not a risk factor independent of alcohol consumption. Despite the link between alcohol and Dupuytren’s disease, the majority of sufferers are not alcoholics. It is suspected that a high risk may be possible from smoking and alcohol having a combination effect increasing the susceptibility of developing the condition.

The condition is more prevalent among people suffering with diabetes, particularly with insulin dependence, although this may be because of the increased severity of insulin dependent diabetes or due to it typically affecting younger patients. Dupuytren’s disease in diabetic patients however often displays a milder form of the disease and is associated with a lower incidence of contractures than in non-diabetics and many of the patients can be treated conservatively. The high prevalence in diabetes may be due to the microangiopathy and increased collagen deposition.

Rheumatoid arthritis demonstrates a lowered incidence of Dupuytren’s disease, yet the role of anti-inflammatory drugs is undetermined, as there is the possibility of the condition masking the deformities characteristically seen in Dupuytren’s disease.

Discussion
Pathophysiology
Little is known about the underlying cause for Dupuytren’s Disease, however the pathology is well recognised in relation to the cellular and connective tissue changes which lead to the condition. Grouped among the fibroproliferative disorder, demonstrating alterations in biochemical and histological make up similar to wound healing. Luck has classified the condition into the three stages of the disease; proliferative, involutional and residual. The proliferation of fibroblasts is a hallmark of the Dupuytren’s disease in the earliest of stages and can resemble malignant processes, like fibroma or fibrosarcoma. This typically clinically manifests as nodules, these nodules expand towards the surface, replacing subcutaneous adipose tissue and attaching to the deep layers of the skin. During the involutional phase the nodules become smaller, firmer and less defined. Myofibroblasts align along the major lines of stress that pass through the nodules, mostly in the longitudinal axis of the hand on the ulnar side. Progression of the condition is characterised by the organisation of the abnormal connective tissue to form cords and the deposition of Type 3 collagen. The involutional stage has many components resembling the processes often seen within scar formation and wound healing. This is in combination with high turnover of myofibroblasts and extra-cellular matrix deposition.

Up-regulation of various growth factors and their receptors are seen in Dupuytren’s tissue, including transforming growth factor (TGF-β1), periostin and basic fibroblast growth factor. Abnormal collagen cross-linkage, together with the contractile forces generated by myofibroblasts,
result in the early formation of contractures. During the residual stage, nodules disappear leaving hypocellular and tendon-like thick fibrous cords. Cords may shorten and become more pronounced, causing further flexion contracture of MCP and PIPJs. The theory of hypoxia and subsequent microvascular damage may go some way to explaining a number of epidemiological associations of the disease.

The mechanism by which the disease progresses from a nodule to a collagenous disease cord is also not understood. Individuals with Dupuytren’s disease, have been shown to have autoantibodies against collagen types I-IV. Often immune cell infiltrates can be seen within the Dupuytren’s nodule, possibly representing an unregulated immune response occurring at this early stage of disease progression.

**Classification**

Tubiana and Michon’s classification or grading system for Dupuytren’s contracture is based upon the combined angle formed by contractures at the metacarpophalangeal joint and the proximal inter-phalangeal joint. Stage N describes the presence of nodules without contracture, Stage 1 is a total flexion deformity from 0 – 45°, Stage 2 from 45 – 90°, Stage 3 90 – 135° and Stage 4 from 135 – 180°. Preoperative proximal inter-phalangeal joint contractures of >60° also have been shown to be prognostic of recurrence after operative treatment. (Figure 1)

**Evaluation**

Assessment of the Dupuytren’s afflicted hand focuses upon the extent of functional limitation as well as the severity of contracture and the involvement of the skin. Skin pitting is due to involvement of the small vertical fibres, or Grapow fibres, connecting the dermis to the palmar fascia. Nodules usually originate in the superficial fibres of the palmo-digital fascia. Several varieties of pathological fibrous tissue can form, resulting in patterns for deformity. Pretendinous cords, from pretendinous bands, result in MCP deformity. Natatory cords, from the ligaments, often limit digital abduction. Central cords result in PIP deformity. Spiral cords can often displace the neurovascular bundle superficially. Lateral cords lead to inter-phalangeal joint contracture. The Hueston table-top test, having the patient attempt to place the hand supine onto the table fully flat, is a valuable functional assessment tool. (Figure 2)

**Treatment**

Unfortunately, there is no curative treatment for Dupuytren’s disease. Most treatment modalities are focusing upon of the abnormal Dupuytren’s tissue from the palm of the hand and the flexor surfaces of the digits. Primary treatment aims is to excise, divide, break or dissolve cords of Dupuytren’s tissue that are preventing full finger extension, thereby releasing the flexion contracture and inhibiting subsequent disease progression. Treatment for Dupuytren’s contracture is often only required when there is functional limitation of the hand. Many asymptomatic cases can be monitored without requiring intervention, however the severity of the contracture will often dictate the treatment option selected.

**Non-surgical treatments**

Non-surgical treatment options for Dupuytren’s contracture include intraliposomal hyaluronidase, trypsin, gamma interferon, triamcinolone, intraoperative topical 5-fluorouracil, external beam radiation, verapamil / nifedipine, but more commonly, radiation therapy and collagenase clostridium histolyticum. All such non-surgical options are generally most effective if used before the condition becomes severe in nature.

**Radiation therapy**

In 2010, the National Institute for Health and Care Excellence (NICE) issued guidance about the use of radiation therapy to treat Dupuytren’s contracture. Radiation therapy aims to produce a total dose of radiation that will result in the ear...
to prevent or delay the need for surgery and is targeted at the nodules and cords within the hand.

The theory behind the treatment modality is the influence of the radiation affecting the development and growth rate of fibroblasts. In one of the studies reviewed by NICE, the symptoms of Dupuytren’s contracture had improved in over half of the hands that were treated after one year.

In another long-term study, two-thirds of people had some degree of symptom relief after 13 years. Complication of radiotherapy being administered to the hand is principally thinning of the skin, however in the long-term a theoretical risk is for the development of skin lesions.

Collagenase clostridium histolyticum
Collagenase clostridium histolyticum (CCH) is the latest treatment modality for Dupuytren’s contracture. Previously, injection of mixtures of proteolytic and anti-inflammatory enzymes including, trypsin, α-chymotrypsin, hyaluronidase, thiomucase, and lidocaine, aiming to disrupt the collagenous environment had been reported to be effective.\(^1,3\)

Collagenase clostridial histolyticum contains two distinct enzymes, class-I clostridial collagenase (Aux-I) and class-II collagenase (Aux-II). These two metalloproteinase enzymes are complementary and synergistic in their ability to digest the highly stable and degradation-resistant triple helical collagen structure. The enzymes act primarily against fibrillar collagen types, including the relevant subtypes seen in Dupuytren cords (types I and III), and lack activity against type-IV collagen, which is found in the basement membrane of nerves, vessels, and skin.\(^3\) CCH targets the NH\(_3\) terminals and COOH internal peptide residues in collagen fibres dissolving the cords.

Current treatment regimens dictate up to three injections can be performed into each cord. The efficacy of CCH injection has been shown to be a successful option in those suffering with moderate severity disease, with up to two affected joints.

Common adverse events following collagenase treatment include swelling, ecchymosis, pain, pruritus, and lymphadenopathy, with 98% of patients experiencing at least one adverse event. Significant adverse events following collagenase treatment include flexor tendon and pulley ruptures are reported to occur in 0.5 – 1.5%. Flexor tendon ruptures are most commonly seen with injection of the little finger, resulting in the recommendation that injections not be placed in the cord > 4 mm distal to the proximal digital flexion crease as the cord becomes closer to the flexor sheath distally in the digit.\(^2\)

Recurrence of disease following collagenase treatment after three-year follow-up was 35% overall, with 27% occurring at metacarpophalangeal joint level and 56% at the proximal inter-phalangeal joints, yet these figures improve if the initial contracture reduction is <5° residual.\(^2\) The major CCH trials, CORD I & CORD II, excluded its use on contractures affecting the thumb. Limited evidence has been published on CCH injection to the thumb, results appear promising.

As with radiation therapy, collagenase clostridium histolyticum is still a relatively new treatment and the true long-term effects are unknown.

Surgical Treatments
Surgical correction of flexion contractures due to Dupuytren’s disease can be broadly divided into four categories: simple fasciotomy, either percutaneously\(^9\) or through small incisions;\(^2\) limited or partial fasciectomy with removal of only the diseased areas of tissue by Hamlin in 1952; total or radical fasciectomy by Skoog in 1948; and dermofasciectomy by Hueston in 1984. Within these broad categories there is further variation.

![Figure 2: Variations of digital band formation patterns.](image-url)
with palmar wounds being left open to heal secondarily by McCash in 1964, longitudinal incisions closed by Z-plasty by McGregor in 1967 or zig-zag incisions closed directly by Bruner in 1967.

**Needle Fasciotomy**

Needle fasciotomy is also known as a needle aponeurotomy or a percutaneous needle fasciotomy. Commonly performed as an outpatient procedure, under local anaesthesia, needle fasciotomy can be a cost and resource effective option, especially for elderly patients or those patients with medical co-morbidities contraindicating more invasive treatment.

However, the rate of recurrence for Dupuytren’s contracture following needle fasciotomy is very high, up to 90% of patients experiencing return of the Dupuytren’s contracture again within three to five years. Complication rates are low, but include skin tears (3.4%), temporary neuropraxia (1.2%), and laceration of the ulnar digital nerve of the small finger (0.1%)36. A much higher complication rate is associated with needle fasciotomy if used in the fingers, therefore it is advocated for use only in the palm to minimise the risk to neurovascular structures.

**Fasciectomy**

A fasciectomy involves removing the thickened connective tissue and can be carried out as a partial fasciectomy, segmental fasciectomy or dermofasciectomy. These are performed in more severe cases of Dupuytren’s contracture, especially in order to achieve more definitive release. Limited fasciectomy is seen to be a more effective treatment in the long-term than percutaneous needle fasciotomy, achieving improvement in 79% of cases versus 63%37. The recurrence rate is far preferable too, with rates around 20-25%. However, there in an increased complication rate, complications including, infection, hematoma, and digital nerve transection, with open fasciectomy in keeping with the more invasive treatment modality and patients recover / return to work faster with percutaneous techniques35.

Modern health care systems are cost and resource driven and it has been deemed not cost effective to perform open fasciectomy or fasciotomy for the single contracture due to the inherent costs of surgery and manpower. However, the surgical cost is balanced out if more than one finger is involved or until such time as CCH costs decrease.(Figure 3)

**Amputation**

In the most severe cases or those of delayed presentation, amputation may be indicated. This is most commonly seen in recurrent disease of the little finger and although this may be the most functionally effective treatment in such cases, complications include; neuroma or neurogenic pain, reduced grip strength and associated cosmetic or psychological issues. (Figure 4)

**Conclusion**

Dupuytren’s Disease, a condition characterized by flexion contracture within the joints of the fingers and hands, is a benign fibroproliferative progressive genetic disorder caused by the formation and deposition of abnormal collagen. Dupuytren’s contracture is a common condition, in particular showing a high prevalence among those of Scandinavian origin.

The condition demonstrates a high genetic predisposition and is associated strongly with alcohol and smoking. Although no curative treatment option exists, the advancements of non-surgical interventions may reduce the necessity for surgical procedures.

However, surgical excision will it seems always play a role, particularly in severe disease.
References


3. Plater F. Observationum in Hominis Affectibus, Volume 3. Basel, König & Brandymuller. This volume can be consulted at the Library of the Wellcome Institute for the History of Medicine, 183 Euston Road, London NW1 2BP, UK 1614.


5. Cline H Sr. Notes of Thomas Smart (student) from a lecture by Henry Cline Senior. Manuscript 29, St Thomas's Hospital Medical School Library, London.


