

Dupuytren's disease

Dupuytren's disease is a common condition of the hand particularly affecting the older population. The cardinal presentation of Dupuytren's disease, is a permanent digital flexion caused by the shortening, thickening and fibrosis of the palmar fascia. The fingers are drawn into the palm, preventing extension of the digits so that simple everyday tasks such as shaking hands or washing oneself become problematic. The restriction in hand function can be very debilitating for the patient and severely impact on their quality of life. There are currently several therapies available for Dupuytren's disease that aim to improve hand function but there remains no cure and it often recurs.

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Dupuytren's disease is a common benign fibro-proliferative disorder characterised by progressive, non-reducible digital flexion and the presence of nodules and cords. Painless nodule formation in the palmar fascia and extension of cords along the digits are the pathological and clinical findings in Dupuytren's disease. Ultimately, as the cord gradually shortens and prevents full extension of the finger, the resultant digital contracture develops. This restriction can severely limit hand function, and consequently has a huge impact on the patients' quality of life. The contracture is the result of shortening and thickening of the palmar fascia (fibrosis) and generally occurs across the metacarpal-phalangeal joints (MCPJ) or proximal interphalangeal joints (PIPJ) whereas distal interphalangeal joint (DIPJ) involvement is seen less frequently.

The rate of development of contracture is variable but generally it takes several years to develop a severe deformity. All fingers can become involved; however the disease most often afflicts the ring

fingers and little fingers.

In some cases, an early sign of Dupuytren's disease can be the dimpling of the palmar skin overlying the diseased tissue due to the thickening and tethering of vertical fascia fibres to the dermis.¹ Pain and itching have also been reported following the formation of the nodule but these symptoms tend to subside.² The patient may report thickened skin in the palm or pain on forcefully gripping objects due to nodules in the palm. Most commonly though, it is the

disfigurement and loss of function, due to the subsequent emergence of the cord, that prompts individuals to seek medical attention.

Dupuytren's disease is common. In Britain, it is thought that 25% of men over the age of 65 years are affected;³ and worldwide, 4–6% of Caucasians are affected.⁴ Although the reported prevalence of Dupuytren's varies vastly between populations (2%–42%), the prevalence is known to increase with advancing age; for males between 45–49 years the prevalence is 7.2%,

Key points

- Dupuytren's disease is a common benign fibro-proliferative disorder characterised by progressive, non-reducible digital flexion and the presence of nodules and cords.
- All fingers can become involved; however the disease most often afflicts the ring fingers and little fingers.
- A predisposition for Dupuytren's disease can be inherited and it seems likely that additional factors such as these contribute to the initiation and development.
- Surgery has long been the gold standard treatment for Dupuytren's disease.
- The most recent promising therapy is clostridial collagenase injection.

increasing to 39.5% in those aged 70–74 years.⁵ In addition to Dupuytren's disease being more prevalent in males it also manifests approximately 10 years earlier in males compared to females, with the highest incidence in the sixth decade for men and in the seventh decade for women.^{6,7}

Dupuytren's diathesis

It has been noted that particular characteristics seem to predispose certain individuals to a more aggressive development of Dupuytren's disease and leave the patient more susceptible to recurrence. This is known as Dupuytren's diathesis, which is defined as "a permanent condition of the body which renders it liable to a special disease."^{8,9} Patients who inherit and exhibit this diathesis have been shown to have a recurrence rate as high as 75%. Listed below are the factors McFarlane¹⁰ and Hueston⁸ established that represent the diathesis of Dupuytren's disease, which more recently have been modified to include age and gender:¹¹

- Young age of onset (before 45 years)
- Male gender
- Bilateral disease
- Positive family history
- Presence of ectopic disease;
- Ledderhose's disease — plantar fibromatosis
- Peyronie's disease—induration and deformity of the penis
- Garrod's knuckle pads—nodular thickenings over the dorsum of the PIP joints.^{11, 12}

Genetic component

Historically, Dupuytren's disease is thought to originate from the



Pictured: Severe bilateral Dupuytren's disease

Viking population that travelled throughout Northern Europe. This accounts for the high incidence of Dupuytren's in areas with a high immigration rate from Northern Europe and also the variable rates observed across other parts of the world. There is certainly a strong genetic component that contributes to the development of Dupuytren's disease as the risk of developing it is 2.9 times greater in those with an affected relative compared to the general population.¹³ Studies have cited autosomal dominant with variable penetrance as the mode of inheritance.^{14, 15}

Aetiology

Normal palmar fascia is primarily composed of type I collagen. However, in Dupuytren's tissue, biochemical analysis has shown there is an increase in type III collagen present, similar to that seen in early wound healing; the major difference being the uncontrolled and persistent manner in which fibrosis occurs in Dupuytren's disease. The excess type III collagen production results from an increased

proliferation of myofibroblasts as a result of an unknown stimulus. This stimulus has been attributed to any one, all, or a combination of the following; oxygen free radicals, narrowed micro vessels, trauma to the palmar fascia, or to an abnormal immune response.¹⁶⁻¹⁸ Other hypotheses suggest thinning of the overlying subcutaneous fat in old age and subsequent reduced protection of the palmar fascia to trauma as a basis for the onset in older people. However, the exact aetiology remains elusive and is likely to be multi-factorial. Currently, several regions of genome have been identified as having an association with the disease and a fuller understanding of the genetics and molecular mechanisms behind Dupuytren's would provide potential scope for the development of curative options.

Risk factors

There is a long list of supposed risk factors for Dupuytren's disease and also a number of associated diseases. Some are well established, but the relationship with other factors

is more unclear, and the related studies often inconsistent.¹⁹

A predisposition for Dupuytren's disease can be inherited and it seems likely that additional factors such as these contribute to the initiation and development. However the contribution of many of these factors remains controversial. Interestingly, only patients with rheumatoid arthritis have been shown to have a significantly lower incidence of Dupuytren's disease.²⁰

Manual labour

The link between Dupuytren's disease and repetitive trauma, including micro-trauma from activities such as climbing, manual labour or operating vibrating machinery is well supported in the literature.^{21,22} In addition, there are case reports of Dupuytren's disease occurring after specific injury to the palm.²³

Diabetes mellitus

A high incidence of Dupuytren's disease has been reported in individuals with diabetes although the severity of diabetes has been shown to have no impact on the incidence.²⁴ The reported prevalence of Dupuytren's disease amongst diabetics varies from 1.6% to 32%.²⁵ The evidence regarding the significance of insulin use is conflicting; some studies show an increased prevalence in insulin dependent diabetics compared to non-insulin dependent diabetics; whereas others have shown there to be no difference.²⁶ The link between diabetes and Dupuytren's is curious. Although Dupuytren's disease is certainly more common amongst patients with diabetes, they tend to have a milder disease progression.²⁷ The higher

prevalence in diabetics is believed to be related to the micro-vessel pathology and increased collagen production that is characteristic of diabetes.²⁸ Interestingly, patients with diabetes have increased rates of other inflammatory and proliferative diseases of the hand and upper limb, including flexor tenosynovitis, carpal tunnel syndrome and frozen shoulder, eluding to a possible shared origin.²⁹

Epilepsy

Since a relationship between Dupuytren's disease and epilepsy was first described, evidence of such a relationship has since been conflicting or recognised as being a result of anti-convulsant use rather than the epilepsy. One study reported the incidence of Dupuytren's to be as high as 56% amongst epileptics.³⁰ However, the effect of either of these factors is regarded as negligible once consulting behaviour is accounted for.

Smoking and alcohol

Cigarette smoking and alcohol are both associated with an increased risk of developing Dupuytren's disease. Furthermore, the excess risk associated with alcohol does not appear to be due to a confounding effect of smoking, or vice versa. Cigarette smoking may be involved in the pathogenesis by producing micro vascular occlusion and subsequent fibrosis and contracture.³¹⁻³³

Management and treatment

Dupuytren's disease is a common hand condition for which a variety

of interventional techniques have been described and applied. Unfortunately, there is currently no cure for Dupuytren's disease. The management of Dupuytren's depends on the severity of the contracture together with the underlying health of the affected individual and how significantly the patient's quality of life is impeded. A key part of patient management is ensuring their expectations are realistic. Counselling patients so that they understand the benefits and limitations of each therapy maximises the chance of achieving patient satisfaction.

Recognising diathesis and counselling patients accordingly regarding management and potential disease course is important.⁸ It is necessary to understand the available interventions, new developments and when each is most appropriate. Current interventions are aimed at restoring function or slowing down disease progression; these can be grouped as operative or non-operative.

Operative

Surgery has long been the gold standard treatment for Dupuytren's disease. Excellent functional results can be achieved with realistic expectations, appropriate surgical intervention and diligence in postoperative recovery and rehabilitation period.

Methods of assessing severity/requirement for surgery have been suggested in the literature ranging from the Hueston's table top test^{34,35} to more rigorous measurements of contractures using a goniometer³⁶ but no definitive threshold of contracture requiring surgery exists.

In making a decision on surgery, the surgeon and patient should be guided by how diminished the patient's hand function is and the consequent reduction in quality of life that the patient experiences.

In the early stages of the disease when the contracture is minimal or progressing very slowly, the risks of having surgery can outweigh the potential improvement in function that may be gained. In these cases, a wait and watch strategy is adopted with monitoring of the disease progression. In severe, recurrent cases or when the patient presents with deformity and impairment that is not conducive to surgical correction, amputation is used as a last resort.

Surgery involves the dissection and/ or removal of diseased tissue, which is often complicated by the involvement of nerves and tendons engulfed in the tissue. The main complication following treatment for Dupuytren's is recurrence.^{37,38} The reported rates of recurrence vary vastly in the literature due to different interpretations of "recurrence" and variable follow-up periods. Nevertheless, the operations are regarded safe and patient satisfaction is largely good.

Complications

The overall rate of complications associated with Dupuytren's disease surgery is around 17%. The 17% of patients who experience complications are more likely to have severe or recurrent disease. An inevitable drawback of surgery is that it results in large scars. Special zigzag incisions (Z-plasty) are used to close the skin in order to prevent scar contracture in the longitudinal plane. Recurrence is a risk with all treatment options although disease extension to other areas of

the hands is the main problem and further surgery may be indicated in the future.

Post-operative care

Pain relief and elevation of the hand is important immediately after surgery to minimise any hand swelling. Post-surgery physiotherapy is strongly recommended and includes daily range of motion exercises to maximise the movement that is restored to the hand.³⁹ A hand therapist will also supply a resting night-time splint to keep the fingers extended at night for six months until the scar has become soft and mature. Patients can generally use their hand for day-to-day activities around two weeks after the surgery. Restrictions or adjustments may be necessary before returning to work that involves substantial use of the hands.⁴⁰

Non-operative

In-line with the general trend towards less invasive treatment options there are many non-operative treatments that have been used in Dupuytren's disease. Non-operative interventions that have been investigated for the treatment of Dupuytren's disease include amoxifen, radiation, ultrasound therapy, vitamin E, physiotherapy, steroid injection, interferon, and splinting.

Perhaps the most recent promising therapy is clostridial collagenase injection. Collagenase clostridium histolyticum (Xiapex) is the first pharmacological treatment to be developed for Dupuytren's contracture and is administered by local injection in the outpatient setting. It is a

combination of two enzymes that work together breaking down the collagen structure of the disease. On day one the collagenase is injected into the diseased cord in the outpatient department. The following day the patient returns to the outpatient department, where, under local anaesthesia, the finger is manipulated straight. The patient undergoes hand therapy as with other Dupuytren treatments. The treatment was given FDA approval in 2010 and UK approval in 2011. Early reports are encouraging and interest is high regarding the long-term effect of repeat injections and contracture recurrence rates.⁴¹⁻⁴³

Collagenase clostridium histolyticum has been the subject of two pivotal studies, Collagenase Option for Reduction of Dupuytren's (CORD I and CORD II).^{43,44} The CORD I study showed that 64% of patients who received injections of collagenase clostridium into the affected digits achieved a reduction in contracture of that joint to five degrees or less, approximately 30 days after the last injection, compared with 6.8% of those injected with placebo ($p < 0.001$).⁴³ In the CORD II study, which had the same primary endpoint as CORD I, statistically significantly more cords injected with collagenase than placebo achieved a reduction in contracture of that joint to five degrees or less, approximately 30 days after the last injection (44.4% versus 4.8%; $p < 0.001$).⁴⁴

As with all treatments for Dupuytren's disease, there are risks associated with the collagenase injections and these will need to be discussed with the patient prior to treatment.

Summary

Dupuytren's disease continues to cause significant functional problems to those patients affected. Early assessment and intervention often yields the best results, as a severely affected digit may not be correctable. The new biologics, in particular the collagenase injections, seem to be offering an attractive alternative to a high proportion of patients affected.

Conflict of interest: none declared

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