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Review Article

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The Role of Mutations on Gene WNT, in Dupuytren Contracture Syndrome

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Abstract

Dupuytren contracture, also known as Dupuytren disease, is a progressive fibrosing disorder of the fingers and palm of the hand. It results in the development of nodules and thickened cords in the palmar fascia that may lead to contractures. In the later stages, structural changes also involve flexion contractures of the joints. Dupuytren contracture is a relatively common disorder that occurs with advancing age. About 5-15% of Caucasian men over the age of 50 years are affected. There is a higher incidence of Dupuytren contracture in younger men than in women, but there is no significant difference in incidence between the sexes by the ninth decade of life. It is rare in Asians and African Americans. Dupuytren contracture may be inherited as a familial condition or it may occur sporadically. The reason for the dose-dependent association of alcoholism and cigarette smoking with Dupuytren contracture is not understood. The incidence of Dupuytren contracture is 2-5 times higher in manual labourers than in-office workers, possibly due to repetitive movements and vibration. The association with epilepsy has been reported inconsistently and may be due to anti-epileptic medications.

Keywords: Dupuytren Contracture Syndrome, Wnt Mutation, Signaling Cell, Progressive Fibrosing Disorder, Finger Hand Disorder

Generalities of Dupuytren Contracture Syndrome

Dupuytren contracture syndrome is a disability in which the joints of one or more fingers cannot be fully extended. Their mobility is limited to a number of flexed positions. These common problems generally get worse over time [1].

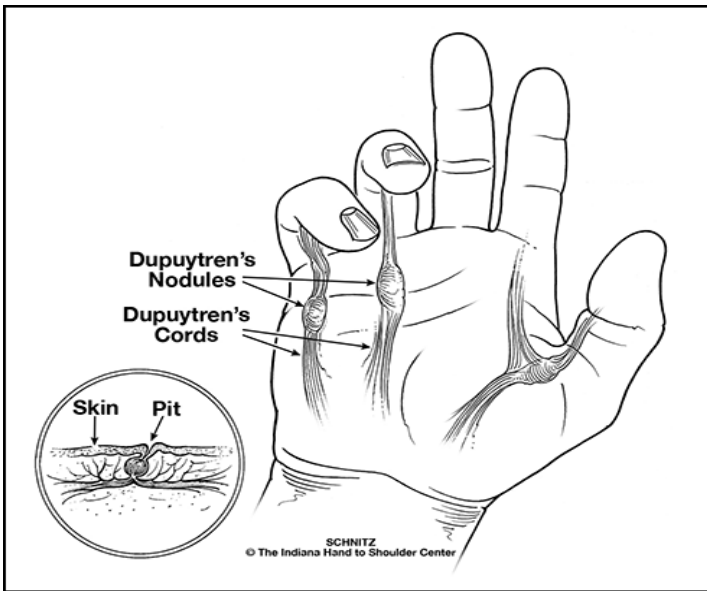


Figure 1: Schematic of fingers with dupuytren contracture syndrome

Clinical signs and symptoms of Dupuytren Contracture Syndrome In men, dupuytren contracture syndrome often occurs after the age of 50. In women, it appears later and is less severe. However, dupuytren contracture can occur at any time of life, including childhood. This disorder can make it difficult for people with handicrafts to perform tasks such as preparing food, writing, or playing musical instruments [1,2].

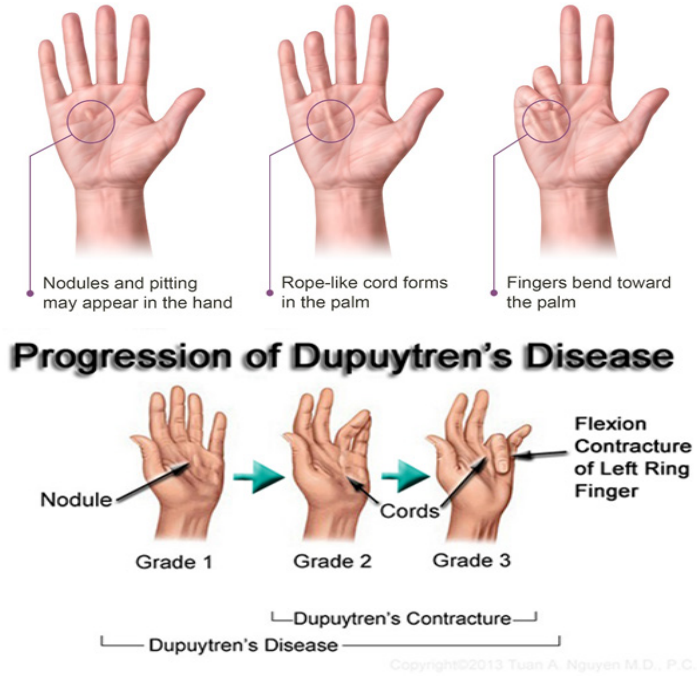


Figure 2: Schematic of the knot disorder in the tissue of the fingers with Dupuytren contracture syndrome

Dupuytren contracture syndrome often occurs initially in only one hand, affecting the right hand twice as much as the left. About 80% of people with this syndrome eventually experience the characteristics of the disease in both hands [1,3].

Figure 3: Images of fingers with Dupuytren contracture syndrome

Dupuytren Syndrome is a connective tissue disorder that supports the muscles, joints, limbs and skin of the body and provides strength and flexibility to body structures throughout the body. Characteristics of Dupuytren contracture syndrome due to shortening and thickening of the connective tissues in the hand include fat and fibrous bands from a tissue called the fascia. It is worth noting that the skin is also involved in Dupuytren contracture syndrome [1,4].

Dupuytren contracture syndrome appears as one or more small tight knots that can be seen and felt under the skin of the palm. In some affected people, the nodules are just a sign of the disorder and sometimes even untreated, but in most cases the condition gradually gets worse. Over months or years, strong tissue bands called ropes develop. These ropes gradually move the injured fingers down so that they touch the palm. As the condition worsens,

it becomes difficult or impossible to move the injured fingers. The fourth finger (ring) is often involved, followed by the fifth (low), third (medium) and second (forefinger). Sometimes the thumb also gets this syndrome [1,4].

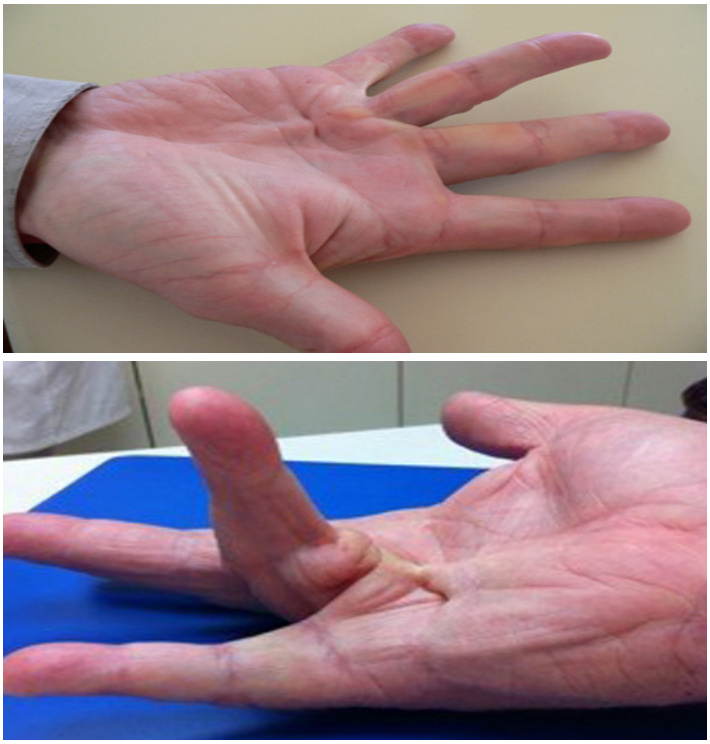
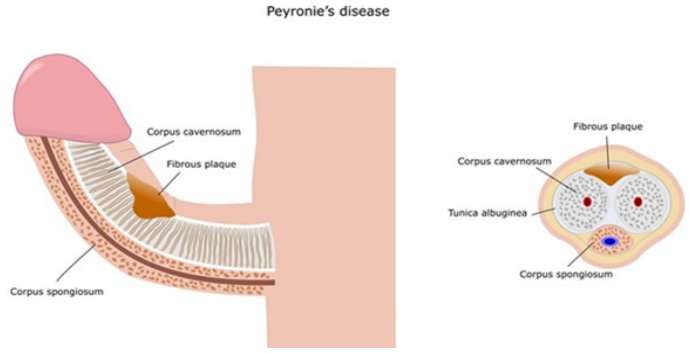


Figure 4: Another view of finger discomfort disorder with Dupuytren contracture syndrome

About a quarter of people with Dupuytren contracture syndrome experience unpleasant inflammation or tenderness, burning or itching in the affected hand. They may also feel pressure or tension, especially when trying to straighten damaged joints [1,5].

People with Dupuytren contracture syndrome are at risk for other disorders in which connective tissue-like disorders affect other parts of the body. These disorders include Garrod pads, which are nodules that develop on the knuckles. Ledderhose disease, also called plantar fibromatosis, affects the foot. Scar tissue in the shoulder that causes pain and stiffness (immobile shoulder). In men, Peyronie's disease causes abnormal curvature of the penis [1,5].



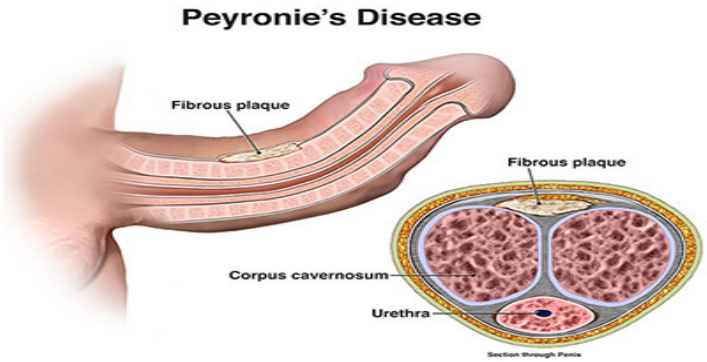


Figure 5: Schematic of the abnormal curvature of the penis (Peyronie's disease) with Dupuytren contracture syndrome

Etiology of Dupuytren Contracture Syndrome

While the cause of Dupuytren contracture syndrome is unknown, changes in one or more genes affect the risk of developing the disorder. Some of the genes associated with this disorder are involved in a biological process called the Wnt signaling pathway. This pathway promotes cell growth and division (proliferation) and is involved in determining specialized cellular functions (differentiation) [1,6].

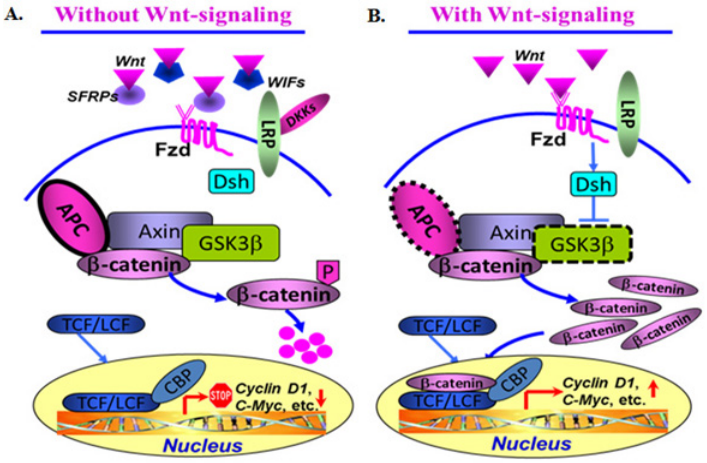


Figure 6: Schematic of the signaling path wnt (B) versus the non-signaling path wnt (A)

Abnormal proliferation and differentiation of connective tissue cells called fibroblasts are important in causing Dupuytren contracture. Fascia are more common in people with the disorder than myofibroblasts, a type of protein that contains fibroblasts known as myofibrils. Myofibrils normally form the main unit of muscle fibers, so they can contract. An increase in the number of myofibroblasts in this disorder causes abnormal contraction of the fascia and overproduction of a tissue protein called collagen type III. A combination of abnormal contraction and excessive type III collagen may lead to changes in connective tissue that occur in Dupuytren contracture syndrome. However, it is still unknown how changes in genes that affect the Wnt signaling pathway are related to these abnormalities and how they are at risk for developing the disorder [1,6].

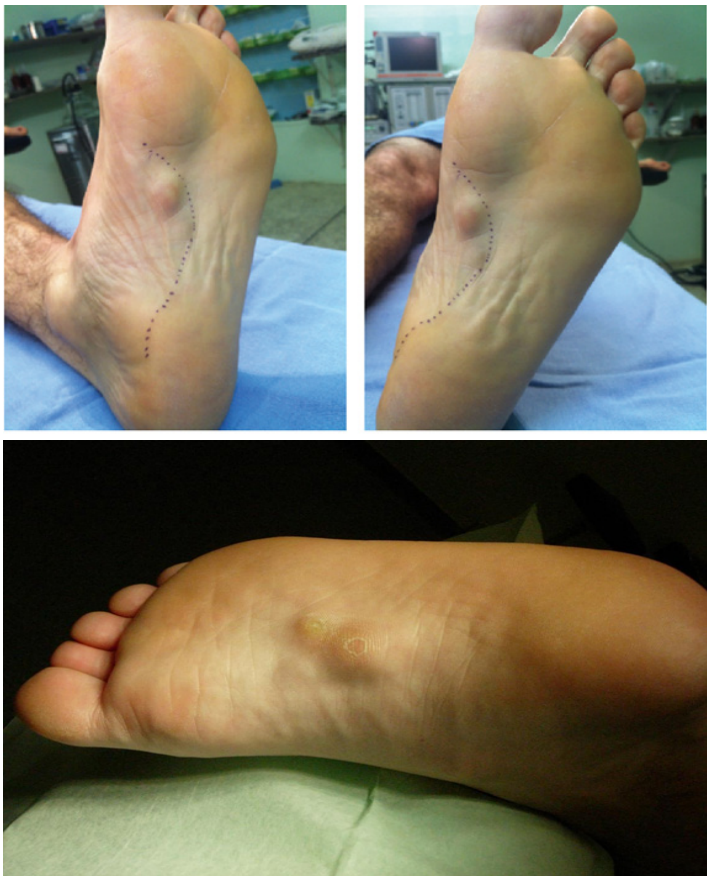


Figure 7: Images of legs with Dupuytren contracture syndrome with Ledderhose disease in the soles of the feet

Other risk factors for Dupuytren contracture syndrome may include smoking, heavy alcohol consumption, liver disease, diabetes, high cholesterol, thyroid problems, and certain medications, such as those used to treat epilepsy and previous injurie [1,6].

Dupuytren contracture syndrome is usually passed down through the family and is the most common inherited connective tissue disorder. The pattern of inheritance is often unclear. Some people who inherit genetic changes associated with Dupuytren contracture never develop the disease [1,7].

In some cases, Dupuytren contracture is not inherited and occurs in people with no history of the disease. These sporadic cases start their symptoms later and are less common in family cases [1,7].

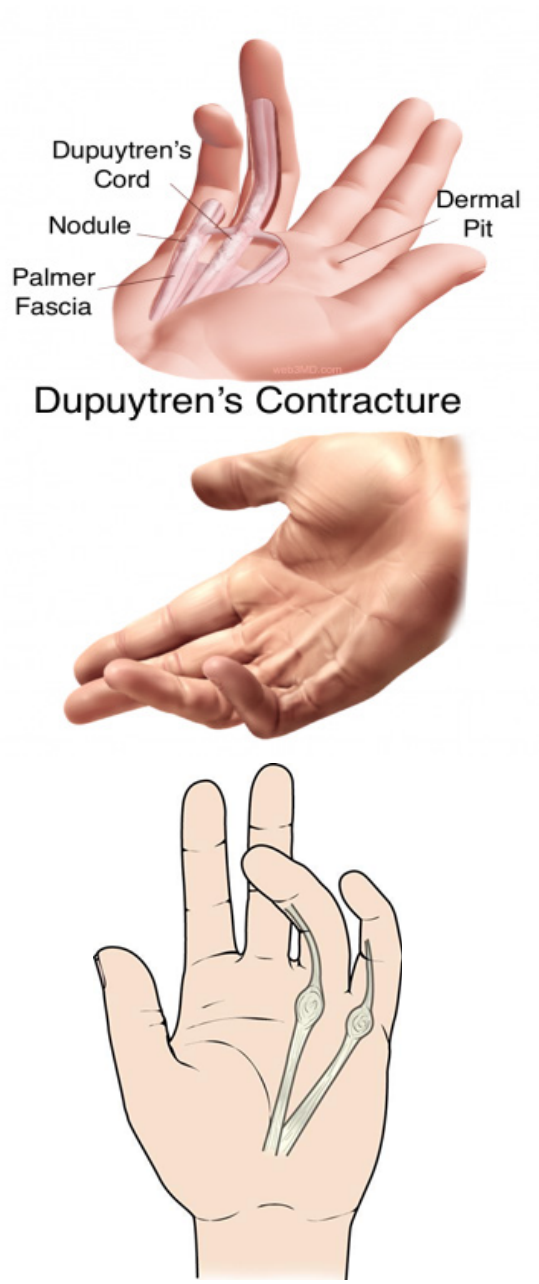


Figure 8: Schematic of the de-smoothing disorder of the fingers associated with Dupuytren contracture syndrome

Frequency of Dupuytren Contracture Syndrome

Dupuytren contracture occurs in about 5% of the US population. These conditions are 3 to 10 times more common in people from Europe than in non-Europeans [1,8]

Diagnosis of Dupuytren Contracture Syndrome

Dupuytren contracture syndrome is diagnosed based on the clinical findings of some patients and some pathological tests. The most accurate way to diagnose this syndrome is to test molecular genetics for want signaling pathway genes to check for possible mutations .[1,9]

Treatment options for Dupuytren Contracture Syndrome

The strategy for treating and managing Dupuytren contracture syndrome is symptomatic and supportive. Treatment may be performed with the efforts and coordination of a team of specialists including an orthopedic specialist, orthopedic surgeon, gastroenterologist, and other health care professionals. There is no reliable treatment for this syndrome and all clinical measures are taken to alleviate the suffering of the patients. Genetic counseling is also essential for all parents who want a healthy baby [1,9].

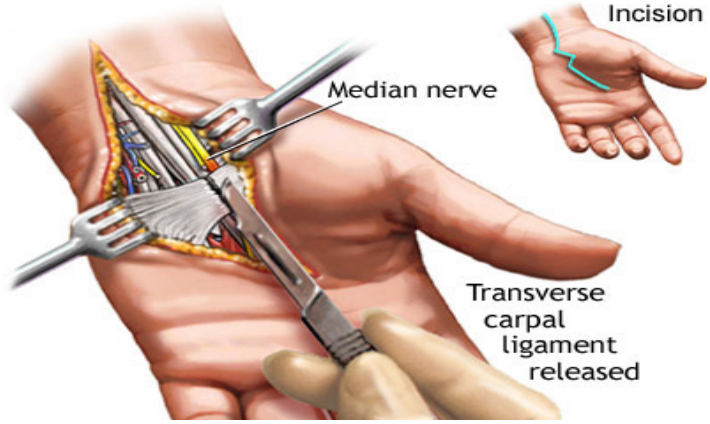
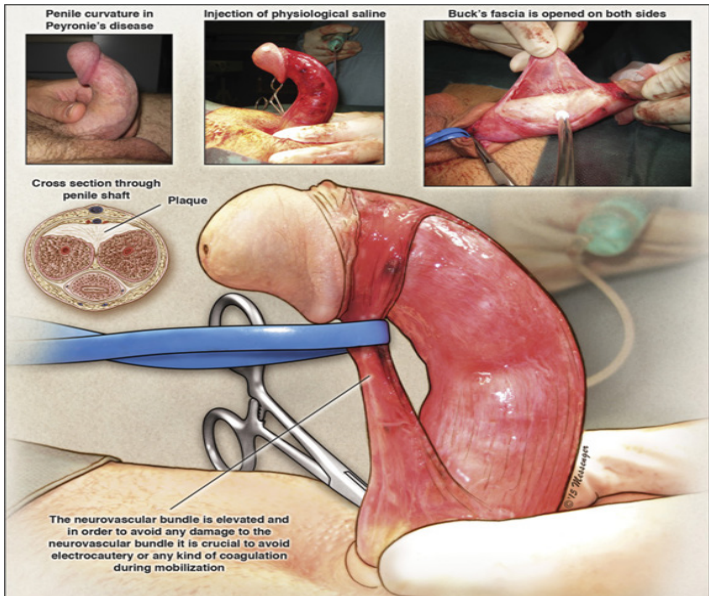


Figure 9: Schematic of surgery for the treatment of fingers with duplex contraction



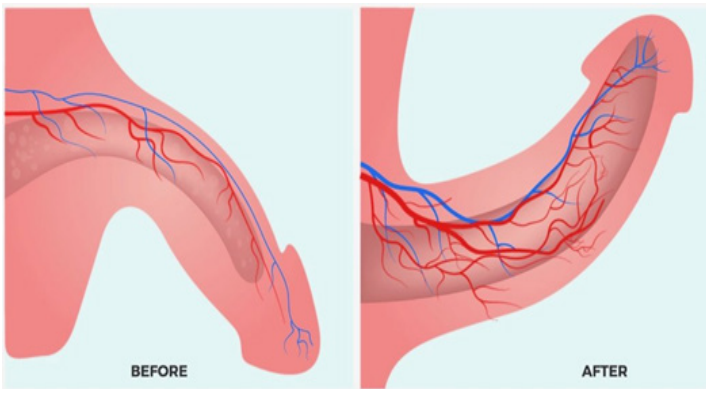


Figure 10: Schematic of surgery to treat abnormal penile curvature with Dupuytren contracture syndrome

Discussion and Conclusion

Dupuytren Syndrome is a connective tissue disorder that supports the muscles, joints, limbs and skin of the body and provides strength and flexibility to body structures throughout the body. Characteristics of Dupuytren contracture syndrome due to shortening and thickening of the connective tissues in the hand include fat and fibrous bands from a tissue called the fascia. People with Dupuytren contracture syndrome are at risk for other disorders in which connective tissue-like disorders affect other parts of the body. Abnormal proliferation and differentiation of connective tissue cells called fibroblasts are important in causing Dupuytren contracture. Fascia are more common in people with the disorder than myofibroblasts, a type of protein that contains fibroblasts known as myofibrils. Non-operative treatment for mild Dupuytren contracture may include splinting (external fixation), which may reduce discomfort and lengthen the neurovascular bundle. It is uncertain if splinting, massage or hand exercises stop the progression of contractures. Surgery is the main treatment for extensive contractures and impaired hand function. Indications for surgery are typically contractures of over 30-40° at the MCP joint and over 20° at the PIP joint. The aim is to restore function to the hands and reverse contractures in the fingers. Limited fasciectomy is indicated for patients with loss of function of the affected hand due to progressive contracture. An isolated lesion with a single cord or band responds better to surgery than diffuse forms of the disease and can be operated on more aggressively. Percutaneous needle fasciotomy is less invasive than fasciectomy and has a fast recovery and low complication rates, but the recurrence rate is up to 65% within 3-4 years. The risks associated with a surgical procedure for Dupuytren contracture include damage to the nerves and flexor tendons and he formation of pseudo-aneurysms (pockets of blood in the bloodstream) [1,9].

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