Dupuytren's disease is a nonmalignant fibroproliferative disease that causes progressive and permanent contracture of the palmar fascia with subsequent flexion contracture of the digits. Although the exact etiopathology in the development of Dupuytren's disease is unknown, certain familial, racial, and physiologic factors have been determined. The latest prospective pathogenesis of Dupuytren's disease are presented.

Dupuytren's disease (DD) is precipitated by a proliferation of contractile fibroblasts and myofibroblasts within the palmar fascia. This fibroplasia causes insidious thickening and adhesion of soft tissue structures, namely fibrous bands and nodules, around tendinoligamentous arrangements deep within the hand. The process subsequently leads to flexion contracture of the digits, particularly the long, ring, and small fingers (Seegenschmiedt, Olschewski, & Guntrum, 2001). The soft tissues within the wrist are not usually involved with overzealous fibroblast production. The fourth and fifth digits are involved more frequently and may demonstrate the earliest progression of digital flexion contracture (Sheon & Anderson, 2004; Wilbrand, Eckbom, & Gerdin, 1999). The most common digit involvement, in descending order, is the little, ring, middle, thumb, and index fingers (Saar & Grothaus, 2000).

**Epidemiology**

Certain populations show a higher prevalence of DD. It is believed that people of “Viking” heritage or the Germanic tribes (McFarlane, 2002) and those of Celtic, Scandinavian, and Scottish descent have a higher propensity for developing DD than persons who are of Afro-American (Aladin & Oni 2001), Asian, Greek, or middle-Eastern descent (Benson, Williams, & Kahle, 2001; Gudmundsson, Arngrimson, Sigfusson, Bjornsson, & Jonsson, 2000). DD is an inherited autosomal dominant trait; however, no specific gene has been identified (Bayat et al., 2002a). The ratio of men to women is 7:1. Dupuytren's disease develops usually after the fourth to fifth decades (Benson et al., 2001; Sheon & Anderson, 2004).

One comorbid medical epidemiologic factor discussed in the literature correlates the microangiopathic complications associated with diabetes mellitus with the development of DD (Arrika, Kontola, & Virkari, 1997; Cagliero, Apruzzese, Perlmutt, & Nathan, 2002; Noble, Heathcote, & Cohen, 1984). Other more commonly documented epidemiologic factors list cigarette smoking, excessive ethanol consumption, and repetitive local mechanical vibratory shock mechanisms as precipitating variables in the development of DD (Bains, 2003; Lubahan, 2003) (see Box 1).

**Box 1**

**Premorbid Medical Conditions That May Be Associated With Dupuytren's Disease**

- Type 1 and 2 diabetes mellitus
- Alcoholic liver disease
- Epilepsy
- Cigarette smoking
- Vibratory manual labor occupations
- Immune system (HLA-DR3, CD-3, CD-6, HIV)
- Genetic susceptibility
- Chronic regional pain syndrome / RSD
- Palmar fascitis associated with malignancy
- Trauma
- Dupuytren’s diathesis: begins in second to third decade, multiple digit and bilateral hand involvement, knuckle pads (Garrod’s nodes), plantar fibromatosis (Lederhose’s disease), and penile fascial involvement (Peyronies’s disease)
- Biochemistry: nitrous oxide; alteration in collagen type I and III; fibronectin receptor dysfunction

Arrika et al., 1997; Bayat et al., 2002, a 2002b; Benson, Williams, & Kahle, 2001; Cagliero et al., 2002; Gudmundsson et al., 2000; Kloen, 1999; Saar & Grothaus, 2000; Seegenschmiedt et al., 2001; Sheon & Anderson, 2004; Thurston, 2003.

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Anatomy and Physiology of the Palmar Aponeurosis

Anatomy

The aponeurosis (palmar fascia) is a thin triangular sheet of dense fibrous connective tissue that covers and forms the terminal attachments of pretendinous bands within the palm of the hand. These spiral-like bands also attach to interosseous muscle fascia called the septa of Legueu and Juvara (see Figures 1 and 2A and B). The bands extend distally to each digit, attaching to the metacarpophalangeal joint capsule and then into the web space architecture that supports the neurovascular bundles in the digits (see Figure 2A and B). The septa of Legueu and Juvara produce seven compartments that contain four sets of digital flexor tendons and three groups of neurovascular arrangements (Benson et al., 2001; Strickland & Leibovic, 1991) (see Figure 3). Other supporting structures within the palm include the transverse palmar ligament and the natatory ligament. There is eventual intertwining and coalescing of terminal extensions of the ligaments and tendons onto soft tissues into the web space. As the fascial sheet extends distally, fibers join to the joint capsule and periosteum and tendon sheaths. Volarly attached fibers are referred to as Grayson’s ligaments, and dorsally attached fiber extensions to the neurovascular bundles are called Cleland’s ligaments.

McGrouther (1982) described the gross microscopic and molecular structural orientation of the palmar fascia. His model explains the presentation of the microanatomy and how diseased fascial tissue extends and attaches into and across the metacarpophalangeal and proximal interphalangeal joints of the hand and digits. The longitudinal fibers within the palmar aponeurosis act as guide channels and retinacular restraining systems similar to a “fibrous skeleton” (McGrouther, 1982). The fibroplasia associated with DD promotes these fibrous band structures to become thickened and cord-like. The longitudinal fibers disseminate from the volar (palmar) structures to the skin. The palmar skin may begin to dimple, pucker, or pit, which indicates the formation of nodules and abnormally thickened spiral-like cords within the palm. Pulling and displacement of the neurovascular bundles toward the midline of the digit may result in nerve injury and possibly the development of complex regional pain syndrome (CRPS), formally called reflex sympathetic dystrophy (RSD) (Lubahan, 2003).

Physiology

Fibroblasts are mesenchymal cells that secrete particular proteins that assist in making connective tissue. These cells reproduce to promote repair of connective tissue structures, e.g., the fascia or aponeurosis as discussed. Overproduction of fibroblasts and myofibroblasts are believed to produce the nodules and eventual cord-like structures that are seen in the palm and digits of the hand with DD. With fibroblast proliferation, the Dupuytren’s nodules and cords become firmly attached or anchored to the flexor tendon sheath, interosseous fascia, joint capsule, periosteum, underlying soft tissues, and skin, creating a puckering or tethering of skin with eventual flexion contracture of the digit, which is pathognomonic for...
Diseased tissue becomes intertwined with healthy tissue, disrupting normal hand-digit functioning.

**Pathogenesis of Dupuytren’s Disease**

DD is characterized by a proliferation of fibroblasts and myofibroblasts. Fibroplasia results in nodular formation and cord-like structures to develop in the digital and palmar fascia (see Figure 3). Dupuytren’s tissue comprises primarily type III collagen and is similar histologically to scar tissue seen in wound healing (Lubahan, 2003; Moyer, Banducci, Graham, & Ehrlich, 2002). It is believed that three stages of cellular overgrowth occur (Bains, 2003; Saar & Grothaus, 2000). The phases are proliferative, involutional, and residual (Bains, 2003; Bayat et al., 2002b; Fitzgerald, Kirkpatrick, & Naylor, 1999; Luck, 1959; Seegenschmiedt et al., 2001). The specific cells associated with DD (fibroblasts and myofibroblasts) sustain sequential hyperplasia over a period of months to years (Fitzgerald et al., 1999). Cellular hyperplasia is genetically stimulated (Bayat et al., 2002a, 2002b; Lubahan, 2003; Thurston, 2003), as well as being histochemically triggered by ischemia/hypoxia of local tissues that cause the production of oxygen free radicals (Gudmundsson et al., 2000; Kloen, 1999; Thurston, 2003) (see Figure 4 and Box 2). Processes that cause the production of oxygen free radicals are excessive ethanol consumption, cigarette smoking, and the human immunodeficiency virus (HIV). Long-term ultraviolet exposure and environmental pollutants also produce free radical damage to the skin and organ systems (Benson et al., 2001). Other substances produced by platelets and macrophages, in response to localized tissue ischemia are cytokines—interleukin-1 (IL-1), tumor necrosis factor (TNF-α), and growth factors, such as platelet-derived growth factor (PDGF-β), epidermal growth factor (EGF), connective tissue growth factor (CTGF), vascular endothelial growth factor (VEGF) (Bains, 2003), and basic fibroblast growth factor [bFGF] (Seegenschmiedt et al., 2001).

Other variables that interplay with the pathogenesis of DD include dyslipidemic conditions seen in liver dysfunction (alcoholic cirrhosis), diabetes mellitus, and seizure disorders (Thurston, 2003). According to Thurston (2003), other factors considered statistically associated with DD are fracture of the distal radius that may precipitate algodystrophy or CRPS, formerly RSD. Manual labor occupations, particularly those that require exposure to repetitive vibration (jack hammers, die-press, etc.) also predispose the local tissues to develop microvascular occlusion and therefore to develop DD (Gudmundsson et al., 2000; Liss &
Stack, 1996; Sheon & Anderson, 2004). Pagnotta, Speechia, and Greco (2002) studied hormone receptors, particularly androgen receptors and their association with DD. Their research defined a relationship between diseased palmar fascia and the upregulation of androgen receptors in a study of male cohorts. Conversely, Hankin, Eckinrode, and Louis (1986) found no connection of estrogen and progesterone receptors in their study of female patients who had diseased (Dupuytren's tissue) within the palmar fascia.

Another area of research has concentrated on discerning a relationship between histocompatibility antigens (human leukocyte antigen [HLA]) and the development of DD. Spencer & Walsh (1984) noted a relationship in the HLA-DR antigen in patients exposed to vinyl chloride who later developed scleroderma and scleroderma-like syndrome (a collagen/connective tissue disease). In contrast, DD is seen less in patients with rheumatoid arthritis (RA), it is believed, because antiinflammatory agents are part of the pharmacologic management of patients with RA (Gudmundsson et al., 2000) and physiologically, antiinflammatory agents inhibit prostaglandin production. Certain prostaglandins cause constriction of the microvasculature and are present in local inflammatory processes.

**Summary**

The cause of soft tissue changes associated with DD are varied and range from mechanical variants that alter cell physiology to free oxygen radicals that also precipitate ischemic changes in cellular biochemistry and normal cellular function and repair. Awareness of premorbid medical conditions and the possible interplay of inherited disease may assist the research and medical communities to develop disease prevention strategies that stem from a genetic basis.

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