

---

---

**Arlan L. Rosenbloom, MD**

*Division of Endocrinology,  
Department of Pediatrics,  
University of Florida,  
College of Medicine*

## **ABSTRACT**

**Diabetes mellitus, both insulin dependent and non-insulin dependent, is associated with limitation of joint mobility of the fingers, which can be due to connective tissue changes, neuropathy, vasculopathy, or combinations of these problems. Distinct clinical problems include Dupuytren disease, flexor tenosynovitis, carpal tunnel syndrome (diabetic hand), stiff hand syndrome, shoulder-hand syndrome (reflex dystrophy) and limited joint mobility (LJM). Stiff hand and LJM syndromes are only seen with diabetes; the others have distinct clinical characteristics in those with diabetes compared to the nondiabetic presentation. LJM is of particular interest because it is common in young patients and associated with an increased risk for the serious complications of nephropathy and retinopathy. Journal of Diabetic Complications 3;2:77-87, 1989.)**

## **INTRODUCTION**

Dupuytren contraction was known for nearly 100 years<sup>1</sup> before an association with diabetes was suggested in 1932.<sup>2</sup> Twenty-three years later, Lundbaek described the stiff hand syndrome uniquely found in middle-aged patients with long-standing diabetes.<sup>3</sup> The associations of diabetes with the carpal tunnel syndrome,<sup>4,5</sup> with flexor tenosynovitis,<sup>6,7</sup> and with periarthrititis of the shoulder and shoulder-hand syndrome<sup>8</sup> were described in the years between 1970 and 1972.

A syndrome of painless limitation of the finger joints, with involvement of large joints and thick, tight, waxy skin, occurring in young patients with insulin-dependent diabetes, initially was described in 1974.<sup>9</sup> This review will concentrate on this condition because it is frequent, does not occur in the nondiabetic young population, and is an important risk factor for other complications, and because a number of biochemical studies have been carried out on biopsy specimens of the associated thick, tight, waxy skin.<sup>10</sup> Furthermore, there is a need for clinicians to recognize the characteristics of the limited joint mobility syndrome (LJM) as distinct from other conditions affecting the finger joints in persons with diabetes. This is particularly important in view of the epidemiologic significance of LJM as a risk marker for microvascular disease, setting it apart from the less common conditions or those that are not uniquely associated with diabetes.

Discussion will focus on the characteristics of each hand lesion, on distinctions between the disease in persons with diabetes as opposed to those without diabetes in conditions which are not unique to diabetes, and on pathogenic hypotheses that may bear on the vascular complications of diabetes.

## **DUPUYTREN DISEASE (DD)**

DD is due to subcutaneous fibrosis of the palmar fascia. In persons who do not have diabetes, there is a 6:1 predominance in men, and DD is only seen in white Europeans. The argument whether or not DD is

Reprints requests: Arlan L. Rosenbloom,  
MD, J-296, JHMHC, Gainesville, FL  
32610.

---

more prevalent in those with diabetes than in those without appears related to the failure to recognize milder expression of DD in those with diabetes. Careful examination demonstrates a 40% incidence in middle-aged patients with diabetes and the absence of a gender difference, reminiscent of the circumstance with cardiovascular risk in women with diabetes. Women with diabetes tend to have knuckle pads, nodules, and skin tethering, without finger joint contracture. Contractures are more radial in the hands of those with diabetes, involving the third and fourth digits predominantly, than in those without diabetes, who typically have involvement of the 4th and 5th fingers. Characteristic lesions may precede the development of diabetes and are present in 16% of newly diagnosed older patients.<sup>11</sup>

Advanced DD lesions requiring surgery have the following characteristics: increased water, type III collagen, and chondroitin sulfate; increased proportions of soluble collagen and reducible crosslinks (indicating synthesis of new collagen); and increased glycosylation of reduced crosslinks. The accumulation of type III collagen and increased hydroxylation and glycosylation of reducible crosslinks are characteristic of granulation and scar tissue.<sup>12</sup>

### STIFF HAND SYNDROME

Stiff hand syndrome is an unusual and incapacitating condition that appears to be due to vascular insufficiency. It was initially described in five patients with long-standing IDDM.<sup>3</sup> Complaints of tingling or a burning sensation in the hand preceded the advent of pain, which was aggravated by movement and led to invalidism in two patients. Subcutaneous tissue of the fingers and palms was stiff and hard, with dystrophic changes of the fingernails in two patients. There was no muscle atrophy. The most characteristic feature was a radiographic appearance of calcification of the arteries of the hand in all five patients. There was a paucity of elastic fibers seen on skin biopsy examination, but no other changes.

### CARPAL TUNNEL SYNDROME

Compression of the median nerve within the carpal tunnel is a common entrapment neuropathy and results in paresthesias of the thumb, index, and little fingers, with pain that is often worse at night. Diabetes accounts for 5–16% of instances.<sup>4</sup> Jung and others<sup>5</sup> described a “diabetic hand syndrome” that appeared to involve both the median and ulnar nerve distribution and was bilateral and symmetrical, affecting all distal and proximal interphalangeal and metacarpal-phalangeal joints. Their 23 patients included 6 who were not taking insulin, with an average age of 43 years and an average diabetes duration of 17 years. In addition to the typical thenar muscle atrophy seen in those without diabetes, there is atrophy of the intrinsic and hypothenar muscles, as well as decreased nerve conduction velocity for both median and ulnar nerves. Thus, in diabetes, this condition appears to be more a neuropathic than an entrapment problem, although connective tissue stiffening and overgrowth could contribute to compression.

### FLEXOR TENOSYNOVITIS

The congenital form of “trigger finger” almost exclusively involves the thumb and is not associated with diabetes.<sup>6</sup> It is estimated that one-third of multiple palmar flexor tenosynovitis in adults is related to diabetes, with a marked predominance in women, a predilection for the right hand, and preferential involvement of the thumb, middle, and ring fingers. This appears to be a connective tissue proliferative problem, with fibrous tissue accumulating in the tendon sheath, particularly where the tendon is constricted as it passes through a fibrous ring or pulley, or over a bony prominence, with swelling occurring distal to the constriction and pain with movement of the swollen segment through the narrowed ring. Crepitus may be palpable or audible with movement and locking can occur in flexion or extension when a nodule becomes impacted.<sup>13</sup>

### PERIARTHRITIS OF THE SHOULDER AND SHOULDER-HAND SYNDROME

Periarthritis, also referred to as adhesive capsulitis, can result from trauma, inflammation, or myocardial infarction and is often associated in these cases with the shoulder-hand syndrome. This has also been referred to as reflex sympathetic dystrophy, causalgia, post-traumatic osteoporosis, or Sudeck atrophy.<sup>14</sup> Diffuse swelling, coldness, erythema, tenderness, and hyperhydrosis of the hand may precede, accompany, or follow the development of thickening of the joint capsule, with adherence to the head of the humerus and marked reduction in the volume of the glenohumeral joint. Swelling and vasomotor instability resolve, with the development of trophic skin changes and contractures. After weeks or months, the tenderness, swelling, and vasomotor dysfunction completely resolve with residual atrophic or dystrophic changes, finger contractures, and occasionally frozen shoulder with atrophy of the shoulder girdle muscles and osteoporosis of the bones of the hand and shoulder.

The clinical picture and natural history is quite different in those with diabetes. Bridgeman<sup>8</sup> found that 11% of 800 patients with diabetes had frozen shoulders compared to 2.3% of 600 age- and sex-matched controls without diabetes. Minimal functional disability was noted among 15 of these patients who had a clinical history of pain for greater than 3 months and had greater than 50% loss of range of motion at the shoulder; their pain was limited to relatively mild discomfort around the shoulder joint.

When patients were selected on the basis of finger joint stiffness, 29 individuals aged 23–65 years, with a diabetes duration of 14–48 years, had a nearly 50% prevalence of frozen shoulder; Dupuytren disease and flexor tenosynovitis were also common, each present in one-third of patients but not thought sufficient to account for the finger joint limitation. Controls who were of the same age and duration of diabetes but were without finger contracture had only a 7% prevalence of frozen shoulder. Bilateralality was present in 10 of the 13, an uncommon circumstance in the spontaneous disease,

where only 5% of cases are bilateral. Half of those with finger joint contraction may have had a form of the stiff hand syndrome,<sup>3</sup> as digital or radial artery calcification was seen in 50% of those with finger contracture versus 14% of controls; there also was a fourfold increase in peripheral neuropathy in those with joint contracture, suggesting a neuropathic component as well.<sup>15</sup> Histologic findings in this study emphasize the difference from shoulder peri-arthritis in those without diabetes. In contrast to the inflammatory reaction with synovial cell proliferation, collagen degeneration, and inflammatory cell infiltration seen in those without diabetes, these patients had histologic findings identical to those described above in Dupuytren disease.<sup>12</sup>

Using less stringent criteria than in the previous study, Pal and others<sup>16</sup> found that 20% of 49 IDDM and 18.3% of 60 NIDDM had shoulder capsulitis in contrast to 5.3% of controls. Half the patients with diabetes of both types had finger joint contracture in contrast to 20% of controls, and the contractures were more severe in those with diabetes; there was no correlation between shoulder and finger joint limitation. The major difference between this study and that of Fisher and colleagues<sup>15</sup> was that the latter eliminated half of their initial patient population because of the joint contractures being obviously due to Dupuytren disease, osteoarthritis, or flexor tenosynovitis. Thus, the lack of correlation between shoulder and finger limitation in the Pal study<sup>16</sup> may be the result of inclusion of numerous patients with other forms of joint limitation.

Among 60 diabetic patients with painful shoulders seen in a rehabilitative population, 25% were found to have decreased working capacity, 42% had restricted hip joint mobility, and recovery was found to be comparable to that of nondiabetic patients with shoulder capsulitis. Thirty-five percent of the shoulders regained nor-

mal mobility, half had clinical limitation, and the rest had functional limitation over a median observation time of 29 months. IDDM was associated with worse prognosis, and nearly two-thirds of these patients had the associated hand syndrome.<sup>17</sup>

### LIMITED JOINT MOBILITY (LJM)

Initially described as a striking limitation of the fingers and large joints, in association with short stature, thick, tight, waxy skin, delayed sexual maturation, and early microvascular complications in 3 older teenagers with long-standing diabetes,<sup>9</sup> LJM was found to occur as a milder manifestation in 8–50% of IDDM studied in the United States,<sup>18–29</sup> Japan,<sup>30</sup> Italy,<sup>31</sup> Ireland,<sup>32</sup> England,<sup>16,33–35</sup> Mexico,<sup>36</sup> Ethiopia,<sup>37</sup> and Hungary.<sup>38</sup> Prevalence depends on the age of the population and the duration of diabetes, as well as on examination technique. The studies are summarized in **Table 1**.

Several reports have described LJM in non-insulin-dependent diabetes as well, as summarized in **Table 2**, with frequencies ranging from 25 to 76%, with the exception of a single study that involved only non-insulin-taking patients.<sup>39</sup>

Gender and race do not influence prevalence. In control pediatric populations, fewer than 2% had stiffness of the 5th fingers only (**Table 1**), while older populations may have as much as 20% involvement, presumably related to occupation and arthritic changes associated with aging (**Table 2**).

Changes typically begin in the metacarpal-phalangeal and proximal interphalangeal joints of the 5th finger and extend medially. The distal interphalangeal joint may also be involved, as may larger joints, most commonly wrist and elbow, but also the ankles and the cervical and thoracolumbar spine. Limitation is painless, nonre-

**TABLE 1 Population-based Studies of LJM in IDDM**

Reference	Age Group	Number	% LJM	Controls		Location
				No.	% LJM	
18	7–18	229	28	201	1	Florida
70	6–26	196	40	124	0	Florida
19	1–18	310	8	199	2	Chicago
30	3–18	68	30	92	1	Japan
20	1–28	309	30	—	—	Florida
31	?	210	9	—	—	Italy
32	5–57	115	36	90	3	Belfast
21	3–22	100	32	—	—	Boston
17	2–16	112	42	50	21	Nottingham
22	5–24	137	19	52	0	New Jersey
36	15–32	34	41	34	3	Mexico City
23	7–23	204	21	90	1	Florida
34	?	215	46	—	—	London, UK
24	?	104	19	—	—	California
25	6–27	311	36	—	—	Florida
26	3–24	95	40	39	3	New York
37	14–62	110	44	300	2	Ethiopia
35	6–39	254	15	110	4	Bath
27	11–83	238	55	45	4	Boston
38	5–18	55	44	—	—	Hungary
28	7–25	375	33	—	—	California
16	18–82	49	49	75	20	Newcastle
29	9–30	211	19	239	0	Florida

TABLE 2 Population-based Studies of LJM in NIDD

Reference	Age Group	Number	% LJM	Controls		Location
				No.	% LJM	
34	?	241	34	—	—	London, UK
58	?	80	45	47	15	Montreal
37	28-79	190	25	300	2	Ethiopia
39	?	165	4	—	—	Italy
27	?	41	76	45	9	Boston
59	mean 55	168	47	100	26M/9F	Scotland
32	34-85	60	52	75	20	Newcastle

sponsive to physical therapy, and nondisabling. Unrecognized cervical spine involvement has been described as complicating endotracheal intubation.<sup>40</sup>

**Examination and Classification** The original method for demonstrating milder LJM was to have the patient place the hand on a flat surface, palm down, with the fingers fanned. The examiner would then determine contact with the plane surface by viewing at table level. The normal hand makes contact with the entire palmar surface of the fingers.<sup>41</sup> A somewhat simpler initial examination technique has been to have the patient attempt to approximate the palmar surfaces of the intraphalangeal joints in a praying position, with the fingers fanned and the wrists maximally flexed (**Figure 1**). Regardless of findings, the examiner should extend the proximal and distal interphalangeal and metacarpal-phalangeal joints. These should extend 180° and 60° respectively, but there may be resistance to the permitted movement. In the absence of definite limitation, this can only be reported as suspicious. Thickening of the tissue surrounding the limited joints and inability to tent the skin may

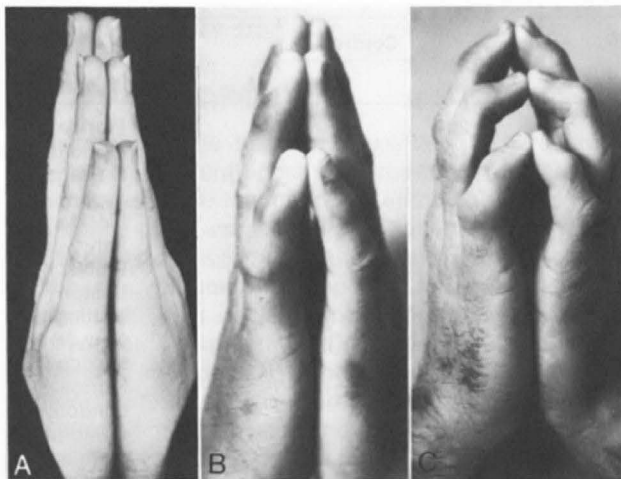
also be noted, particularly over the dorsa of the fingers and metacarpals. Maximal passive extension of the wrist should be at least 70° and of the elbow at least 180°. Cervical spine lateral flexion should permit ear to shoulder, and thoracolumbar spine lateral flexion should be at least 35° in young patients.<sup>41</sup>

This examination will reveal obvious limited joint mobility but, as noted, the clinical sensation of joint limitation without absolute reduction in maximum extension is highly subjective. Buithieu and associates<sup>29</sup> compared metacarpal-phalangeal (MCP) and wrist maximal extension in 239 controls and 211 IDDM aged 9-30 years, and found a significant proportion of those without clinical LJM by the above examination to have MCP and wrist limitation, defined as less than 2 standard deviations of the control mean. Those without LJM (n = 172) included 25% with MCP limitation and 13% with wrist limitation. Thus, earlier detection of LJM may be possible through objective measurement.

The staging of LJM has been useful in describing relationships of other findings to LJM and for patient follow-up. "No limitation" includes equivocal or unilateral findings. "Mild LJM" indicates involvement of one or two proximal interphalangeal (PIP) joints, one large joint, or only the MCP joints bilaterally. "Moderate limitation" refers to involvement of three or more PIP joints, or one finger joint and one large joint bilaterally. "Severe LJM" refers to obvious hand deformity at rest or associated cervical spine involvement.<sup>20</sup>

The term "juvenile diabetic cheiroarthropathy" was applied to 11 patients with severe LJM reported by Benedetti and Noacco<sup>42</sup> in 1976. This terminology is inadequate in view of the involvement of large joints, in addition to the hand, and the implication that the joint itself is involved, which is not the case; radiographs of the joints fail to reveal any intrinsic abnormality, only the periarticular thickening.

**Natural History** Duration of diabetes is the most important variable in the expression of LJM in cross-sectional studies. This is important because it has led to the conclusion that the association with long-term complications is simply that both are related to duration.<sup>26</sup> However, when the time of development of joint changes can be estimated, attained age is more important than duration of diabetes.<sup>43</sup> In a group of 76 patients with age of onset varying from infancy to adolescence, development of LJM occurred between ages 10 and 20 years in over



**FIG. 1** Normal approximation of palmar surfaces of finger joints of 20-year-old with diabetes of 9 years duration (**A**); limited ability to fully approximate the palmar surfaces of the finger joints because of stiffness of all proximal and distal interphalangeal joints in 16-year-old with diabetes for 11 years (**B**); severe limitation in 26-year-old with 24 year history of diabetes (**C**). (Reproduced with permission.<sup>43</sup>)

90%. Of 15 patients with onset of diabetes at under 4 years of age, none developed LJM before 11 years; this was indistinguishable from children with later onset diabetes. When the population was evenly divided between those with onset under and those with onset over 7 years of age, there was a 2.5 year difference in the mean age of LJM onset despite a 6.3 year difference in the mean age of onset of diabetes.

The interval between detection of mild LJM and progression to moderate or severe changes varies from 3 months to 4 years, with a mean of 2 years. Following this period, progression, if any, appeared to be very slow. Many do not progress beyond the mild changes. In adult populations, two-thirds of affected patients will have at least 2 fingers involved.<sup>32,34</sup> One-half of young patients with greater than 5 years duration of diabetes who have LJM will have moderate or severe changes, and approximately one-third of the affected group will have severe limitation.<sup>20</sup>

**Relationship to Diabetes Control** Among the controlled studies, no relationship of LJM to metabolic control of diabetes has been demonstrated, using either glycosylated hemoglobin levels or clinical criteria. However, longitudinal data from the time of diabetes onset have not been studied in relationship to the development of LJM. The more severely affected patients have had hepatomegaly.<sup>31,41</sup>

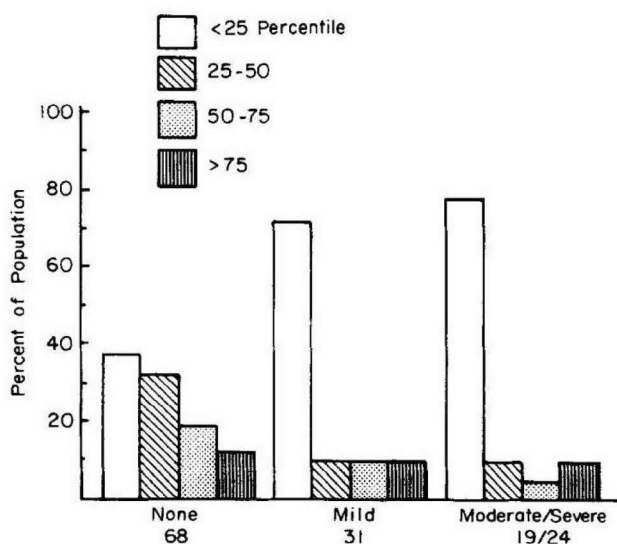
**Effects on Growth** Growth failure and delayed sexual maturation were striking features in the initial patients described with severe LJM.<sup>9,42</sup> Subsequent study in a larger population confirmed the association of severe LJM with growth limitation, but this was not seen with mild LJM.<sup>41</sup> In individuals who had greater than 3 years duration

of diabetes and onset preceding adolescence, thereby permitting sufficient time for growth failure to occur, all stages of LJM were seen to be associated with growth impairment.<sup>43</sup> Of 142 youngsters studied, 31 had mild LJM and 43 more severe changes. Without LJM, 68% were below the 50th percentile, rather than the expected 50%, and most of this discrepancy was in the group below the 25th percentile (38% versus the expected 25%). Mild LJM resulted in four times the excess below the 25th percentile (72%) and moderate to severe limitation did not significantly worsen this picture (**Figure 2**). It is interesting that the small proportion above the 75th percentile was similar without, with mild, or with severe LJM.

**Differential Diagnosis** The characteristic features of LJM, particularly as it appears in the young patient, should result in little or no diagnostic confusion. There is no other condition that results in painless, non-inflammatory limitation of the hand and larger joints in young persons. Rheumatoid arthritis (RA) is not more frequent in diabetes, and patients with LJM do not meet the pain or inflammatory criteria for RA.<sup>41</sup> LJM is easily distinguishable from DD, the only other condition associated with diabetes and involving the hand that is not associated with pain, by the absence of palmar fascial thickening and nodules, as well as by the fingers involved. DD is not seen in young patients. In older patients, DD and LJM may be seen together. All the other conditions affecting the hand in diabetes are associated with pain and other characteristic findings, as noted in **Table 3**. Despite the ease of differential diagnosis, some have lumped together these various conditions as LJM, or considered them to be varying manifestations of the same process, which could be true only in such a broad sense as to be meaningless.

There have been a number of examples of diagnostic confusion in the literature. A recent textbook of diabetes describes only LJM in a section entitled "Stiff Hand Syndrome."<sup>44</sup> The report of LJM preceding the development of diabetes by 3 years in a teenage patient<sup>45</sup> suggested an important constitutional component to recent reviewers of connective tissue complications of diabetes.<sup>13</sup> However, the patient described had developed stiffness in the MCP and PIP joints and wrists more or less simultaneously, had thickening and contraction of flexor tendons in the palm, and experienced progressive disability. Robertson and others<sup>46</sup> described a patient in her late 20s with characteristic features of flexor tenosynovitis, but she was reported as having "juvenile diabetic cheiroarthropathy." Three patients reported as having LJM appeared to have the carpal tunnel syndrome (diabetic hand syndrome), with additional features of shoulder-hand syndrome in one and flexor tenosynovitis in another.<sup>47</sup>

Superimposition of other hand syndromes on LJM as patients age would not be surprising.<sup>17</sup> Under these circumstances, the original LJM problem may be difficult to distinguish, but the presence of pain or paresthesias, neurologic findings, disability, finger locking, swelling, muscle atrophy, palmar skin or fascial thickening, or absence of greater involvement of the 4th or 5th fingers,



**FIG. 2** Distribution of height percentiles in 142 children with diabetes onset before puberty and of 3 or more years duration according to severity of LJM. Reference data is from the National Center for Health Statistics growth charts; distribution should be equal for each of the bars. (Reproduced with permission.<sup>43</sup>)

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.