

## II. Fibrosis in disease

CHAIRMAN: C. LEVENE

### Keloid and Dupuytren's contracture

JAMES CALNAN

*From the Department of Plastic and Reconstructive Surgery, University of London, Royal Postgraduate Medical School and Hammersmith Hospital, London*

April 23 is St. George's day, so the organizers of this symposium very commendably decided to sort out that particular medical dragon called 'fibrosis'. But why lump keloid and Dupuytren into one paper? The reason will become all too obvious—ignorance. It is a curious paradox in medicine that we take longer to tell the things we do not know than those that we do. I would like to present both conditions and discuss the main points under four headings.

#### What features are common to both?

The similarities in the two conditions may be listed as follows: (1) originally described in France; (2) most cases symptomless; (3) histology uninformative; (4) explanations numerous; (5) cause unknown; (6) recurrence common.

(1) Both conditions were described by Frenchmen over 100 years ago. Today we understand neither. Baron Dupuytren produced a classification of burns which is long forgotten. He is remembered for a peculiar condition of the hand because we have no more suitable name (1834). Dupuytren disease (what kind of disease?) or Dupuytren contracture (but there may never be any contracture) are meaningless terms—they tell us little except to bring a visual picture to mind (Figs. 1, 2, 3, 4). Alibert (1806) described keloid in 1825—the fabricated name from Greek meaning 'tumour-like'—although he had already recognized the entity in 1806.

(2) Both conditions are common, most cases are symptomless. Heuston (1963) noted that the incidence of Dupuytren in men aged over 55 years was 10% in the general population, rising to 18% at 75 years. Comparable figures for women were 2% and 7%. The incidence of keloid is not known with any accuracy.

(3) The histology is uninteresting and uninformative (Figs. 5, 6). Cosman *et al.* (1961) believed

that hyalinization of collagen fibres, as shown by deeply eosinophilic staining without obvious structure, was diagnostic of keloid. I agree, but this is not always seen and may require serial sections to show it. In Dupuytren similar structureless areas

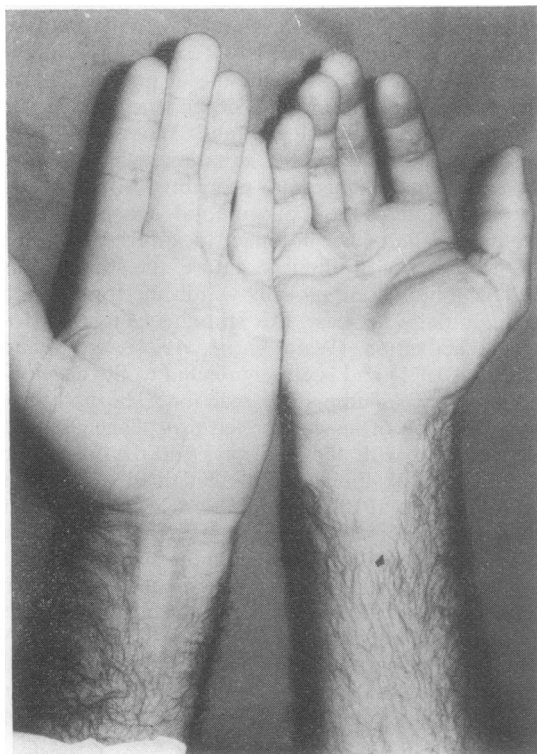


FIG. 1 Dupuytren in 60-year-old farmer. Left hand treated by local excision one year previously: now general flexion of digits 3, 4, 5 of right hand with tethering of skin in palm

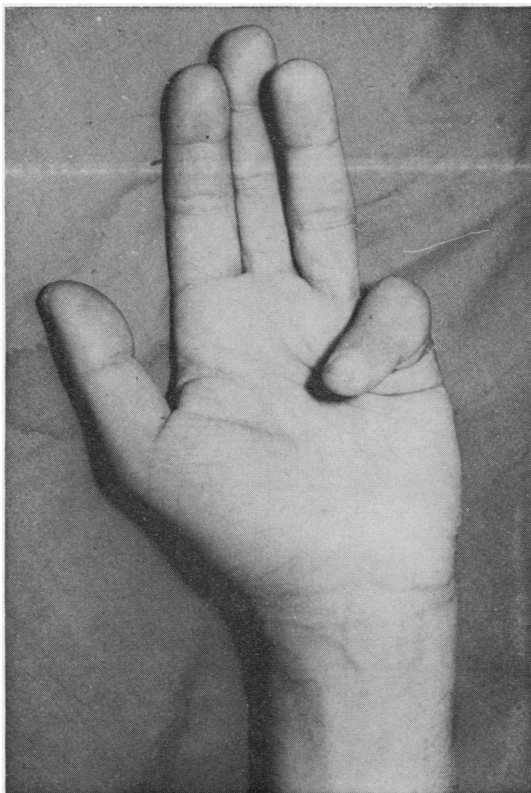


FIG. 2 Severe contracture of left little finger in 52-year-old salesman. Fibrotic bands almost entirely limited to that finger with little in palm



FIG. 3 Knuckle pads over the proximal interphalangeal joints of all fingers of left hand of 56-year-old housewife. Only index finger on right hand has knuckle pad



FIG. 4 Same patient as in Fig. 3. Only palmar thickening over metacarpophalangeal joint of little finger of right hand and no contracture of that digit (arrow). Thickening had been present for 5 years. Knuckle pads originally diagnosed as Heberden's nodes of osteoarthritis

may be seen, but what do they mean? Earlier, Garb and Stone (1942), reporting on 80 patients in detail, had the same difficulty in diagnosing and differentiating between hypertrophic scars, syphilis, tubercle, sarcoid, scleroderma, paraffinoma, and fibroma. Really only the first and last in the list are relevant. In keloid they noted that collagen fibres were densely packed—but so they are in Dupuytren. It is interesting to note that 30 years ago intrakeloidal injection of fibrinolysins were condemned—how fashions change!

(4) Explanations for both conditions are multiple and plausible. Despite excellent monographs on Dupuytren contracture (Skoog, 1948; Hueston, 1963; Stack, 1973) and several theses on keloid which I have had to read we are none the wiser.

(5) The cause of both conditions is unknown, but research of a sort continues. Noticeably most communications contain many references while adding little to knowledge. For example, Garb and Stone's (1942) had 60, Griffith's (1966) 20, Ketchum *et al.* (1966) 66, and Calnan's (1963) 50—many of which were repetitious. Most explanations of the aetiology are anecdotal and speculative at best; even this paper is not exempt.

(6) Recurrence after surgical excision is common. With keloid the figure is probably 80%, for Dupuytren less than 30% (Boyes, 1970). In all, published papers indicate a rather disquieting and disappointing picture of aetiology and management.

#### What features are dissimilar?

To my mind there are five main dissimilarities in the two conditions, although the evidence is slim and most of it is simple testimony. They are as



follows: (1) geography and race; (2) site; (3) age and sex; (4) familial; (5) special factors.

(1) The geographical distributions differ, for Dupuytren seems to be much commoner in White races and keloid a disease of the Negro. There have been very few population studies, so it is difficult to be sure. For instance, Naegeli (1931) reported an incidence of 4.5% of keloid in vaccination scars in 1055 school children in Switzerland, but 13% of 834 adults. Yet Staub (1931) found keloids in 16% of 1205 adult Congolese—a figure not much different from the white-skinned Swiss. Even so, Cosman *et al.* (1961) found keloid to be three times commoner in Negroes in 247 patients with keloid in a New York hospital.

(2) The site of keloid formation shows a predilection for the head and neck. It is rare on the palm of the hand or the sole of the foot, but may

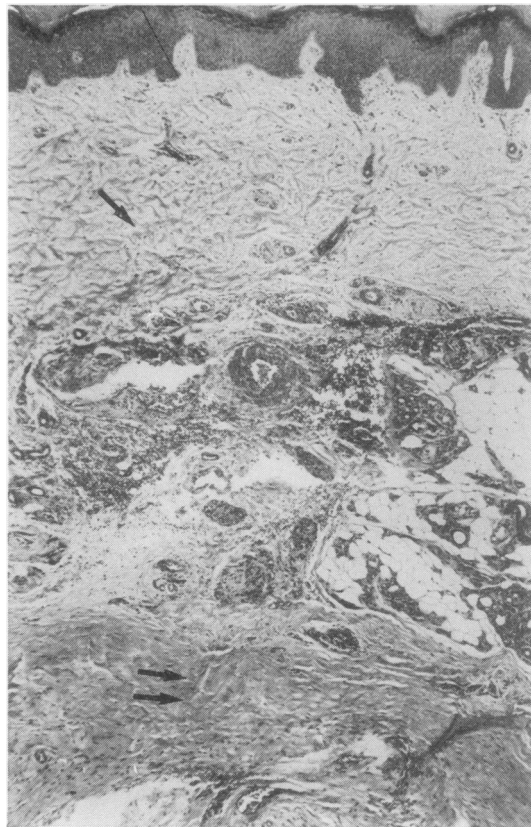


FIG. 6 *Histology of Dupuytren nodule in palm of 35-year-old typist. Compare with Fig. 5: note blunted rete pegs of epithelium, amorphous areas in dermis (arrow), and deeper fibrotic dense layer (arrows). Haematoxylin and eosin.  $\times 60$*



FIG. 5 *Histology of keloid from ear lobe of 20-year-old West Indian woman, present for 5 years, occurring at least 10 years after ear-piercing. Note flattened, blunted rete pegs of surface epithelium and untidy collagen bundles and amorphous areas (arrow) in dermis. Haematoxylin and eosin.  $\times 60$*

occur anywhere (Fig. 7). Dupuytren, on the other hand, is limited to the palmar fascia, but 5% of those affected will have knuckle pads over the proximal interphalangeal joints of the fingers (Fig. 3), 5% have plantar nodules, and 3% develop Peyronie's disease of the corpora cavernosa.

(3) Dupuytren is common after the age of 50 years, occurring 'naturally' in more than 10% of the male population of Australia, according to Hueston (1963), yet keloid, although rare in infants and the very old, may occur at any age. Dupuytren is seen in six men for every woman affected; keloid in slightly more women than men, possibly because of the use of earrings (35% of all keloids referred to hospital occur in the ear lobes).

(4) Dupuytren seems to be familial in 16%–68% of cases (Boyes, 1970; Early, 1962). In about half of those affected it is bilateral. There is not often a family history in keloid.

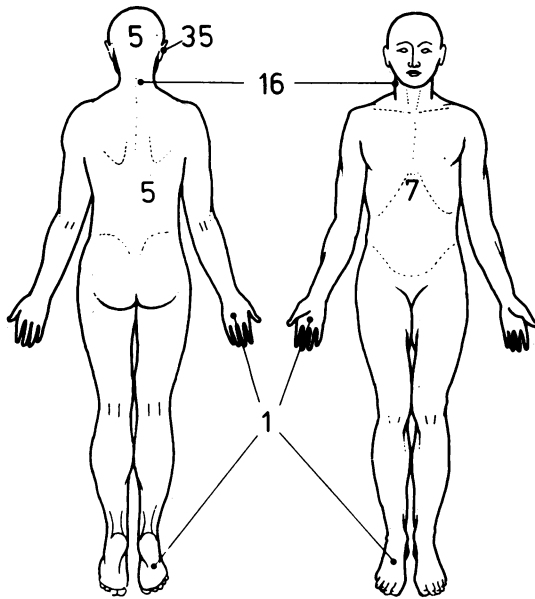


FIG. 7 Diagram to show percentage incidence of keloid according to site

(5) Other factors have been implicated in the aetiology. Dupuytren seems to be commoner in diabetics and alcoholics. Epilepsy gets blamed for several ill-understood conditions and Dupuytren has a share. Early (1962) found 4% epileptics in 620 patients and Hueston (1963) 5.2% in 42 patients, whereas the incidence in the general population is only about 0.4%. Trauma is blamed for both conditions, but can this be so? The hands probably receive more trauma than anywhere else on the body, but keloid there is rare. Moreover, Dupuytren is found as often in professional people (such as pianists, doctors, accountants) as in manual workers. Also the fingers commonly affected are in inverse order to those most liable to trauma (Fig. 8).

Although a history of specific trauma is uncommon keloid in pierced ears seems to support the current hypothesis. However, it must be pointed out that the interval between cause and effect may be as long as 10 years, which is strange.

### Management

Again we can compare and contrast what has been recommended in the past. For Dupuytren there have been mild, moderate, and radical surgery; manipulation and splints; and vitamin E. For keloid there have been shaving, grafting, and excision; pressure; corticosteroids; hyaluronidase; radiotherapy; and vitamin E. Masterly inactivity has been employed for both.

The correct word is 'management' not 'treatment', certainly for keloid. Few experienced surgeons now try excision alone. From advising radiotherapy before and after operation (Levitt and Gillies, 1942) fashion has moved to simple shaving of the tumour portion, then to skin grafting the site after excision, and now concentrates on such simple measures as constant pressure and the injection of corticosteroids.

Griffith (1966) popularized the intrakeloidal injection of triamcinolone acetonide, reporting good results in 56 patients. But the follow-up period was short, for Cosman *et al.* (1961) had already shown that keloid may recur up to 4 years afterwards. In the same issue of *Plastic and Reconstructive Surgery* in 1966 Ketchum *et al.* reported on the treatment of 195 patients with hypertrophic scars, keloid, and scar contracture with the same corticosteroid. Again, results were most promising. However, Scroggins and Kliman (1965) had warned of the systemic effects of absorption, which were noted in patients having surface application of triamcinolone under an occlusive dressing. Furthermore, Fisherman (1962) found in 27 patients that triamcinolone acetate caused depressed, non-tender areas in the skin and subcutaneous tissues after injection (similar to the lipodystrophy after insulin injection) and thin atrophic skin. The popularity of vitamin E given systemically (it is unpleasant to take, anyway) has waned. Needless to say, results are disappointing.

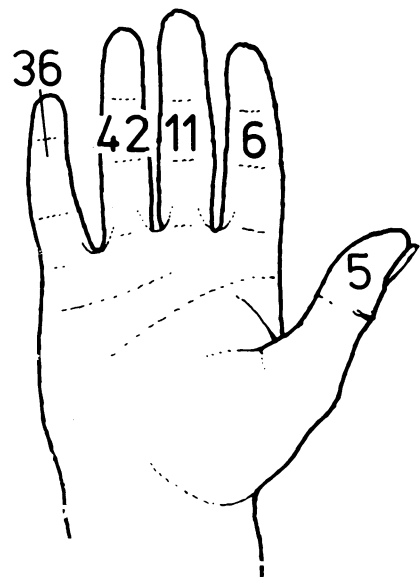


FIG. 8 Diagram to show percentage incidence of fingers affected by Dupuytren, based on a total of 3850 digits (2612 hands) reported by Boyes (1970)

Surgical excision has something to offer for Dupuytren (Clarkson and Pelley, 1962) provided the contracture has not flexed any single digit quickly or for long. The wide-ranging and radical excision of all the palmar fascia has given way to much more localized removal with, I think, better long-term results. Even so the beneficial effects of operation tend to deteriorate with time; Hueston (1963) found that 69% 'excellent' results had fallen to 49% after 10 years.

Knuckle pads (first described by Garrod in 1904) present no problem unless the extensor tendon is inadvertently damaged during excision by an inexperienced surgeon. Plantar nodules do reasonably well, but patients with Peyronie's disease are usually worse off from excision of the plaques of scar tissue. On the whole, it is wise not to operate on a hand unless there are good indications. Evidence that we observe this rule comes from our own performance. For a district with a population of about 100 000 there should have been 40 operations a year, yet we have treated only 60 patients in 6 years, mostly as out patients (Table). Masterly inactivity is still the most popular treatment for both conditions.

**Table** Operations for Dupuytren contracture at Hammersmith Hospitals serving population of about 100 000

Year	No. of operations		Percentage as outpatients
	Expected	Actual	
1970	40	15	30
1971	40	12	70
1972	40	7	50
1973	40	4	100
1974	40	10	50
1975	40	12	70
<b>Total</b>	<b>240</b>	<b>60</b>	<b>62</b>

### The future

I am now fairly certain that neither condition occurs in animals, having looked for and specifically tried

to produce keloid in them without any success. In man proline hydroxylase and collagenase activity in keloid skin are both substantially raised (Chvapil, 1975; Cohen *et al.*, 1975) and it has long been recognized that enzymes such as acid phosphatase, which are found in the skin of normal healing wounds until about three weeks, may still be present in a keloid of many years.

Fifteen years ago I transplanted three Dupuytren's specimens from the palm to a subcutaneous pouch at the wrist and within a year all the implants had disappeared. Eleven keloids transplanted from the affected site to the anterior abdominal wall all flattened and softened to become normal skin. In six cases in which the abdominal skin was cross-grafted to the keloid area the skin grafts became keloid (Calnan, 1963)—an indication that keloid is 'site determined'. But of what clinical use is such information?

Perhaps the best hope for the future lies in multi-disciplined symposia such as this where ideas can be pooled even if resources cannot. The real difficulty lies in diagnosis, for neither condition has special features of pathology. In this respect, the paucity of publications in the 1970s is indicative of our failure to differentiate one condition from the other. To the pathologist the site of origin is imperative for his written report. 'Dupuytren' in the palm of the hand, 'keloid' elsewhere. For the clinician the same applies.

The other difficulty is that neither keloid nor Dupuytren seem, at least on clinical grounds, to be single disease entities. In many patients Dupuytren is not a progressive condition, while in a few the fingers are pulled down into the palm within a year, are not straightened completely by surgical operation, and palmar thickening recurs shortly. It may also occur, rarely, in rheumatoid arthritis, when the main symptom is inability to *flex* the fingers. There are keloids which progress in area and protruberance relentlessly, while others remain stationary for years. And why do some keloids itch when first they appear while others do not?



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