

Journal of Hand Surgery (British and European Volume)

<http://jhs.sagepub.com/>

The Presence of Myofibroblasts in the Dermis of Patients with Dupuytren's Contracture : A possible source for recurrence

B. G. McCANN, A. LOGAN, H. BELCHER, A. WARN and R. M. WARN

J Hand Surg [Br] 1993 18: 656

DOI: 10.1016/0266-7681(93)90029-F

The online version of this article can be found at:

<http://jhs.sagepub.com/content/18/5/656>

Published by:



<http://www.sagepublications.com>

On behalf of:

[British Society for Surgery of the Hand](#)



[Federation of the European Societies for Surgery of the Hand](#)



Additional services and information for *Journal of Hand Surgery (British and European Volume)* can be found at:

Email Alerts: <http://jhs.sagepub.com/cgi/alerts>

Subscriptions: <http://jhs.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.com/journalsPermissions.nav>

Citations: <http://jhs.sagepub.com/content/18/5/656.refs.html>

>> [Version of Record](#) - Oct 1, 1993

[What is This?](#)

THE PRESENCE OF MYOFIBROBLASTS IN THE DERMIS OF PATIENTS WITH DUPUYTREN'S CONTRACTURE

A possible source for recurrence

B. G. McCANN, A. LOGAN, H. BELCHER, A. WARN and R. M. WARN

From the Departments of Histopathology and Plastic Surgery, Norfolk and Norwich Hospital, and the School of Biological Sciences, University of East Anglia, Norwich, UK

Samples of skin and underlying cord obtained at dermofasciectomy for Dupuytren's contracture have been examined for the presence of smooth muscle α -actin (SM α -actin), a marker for myofibroblasts. 15 of the 20 samples stained positively for SM α -actin corresponding with areas of hypercellular Dupuytren's tissue. In 12 of these 15 samples SM α -actin-positive hypercellular Dupuytren's tissue extended into the dermis, in three cases reaching the epidermis. In eight samples, diffusely distributed cells positive for SM α -actin and resembling fibroblasts were seen in the dermis. These cells appeared to be separate from the Dupuytren's foci. The presence of hypercellular foci and isolated fibroblasts positive for SM α -actin within the dermis may explain the high recurrence rate of Dupuytren's disease after fasciectomy.

Journal of Hand Surgery (British and European Volume, 1993) 18B: 656-661

Recurrence after Dupuytren's surgery is common and occurs in more than 50% cases after fasciectomy (McGruther, 1990). There is evidence to show that myofibroblasts have a major role in the development of the disease (Schurch et al, 1990). Using antibodies

against SM α -actin as an immunological marker for the presence of myofibroblasts (Skalli et al, 1989) we have looked for their presence in the subcutis and dermis removed at dermofasciectomy.

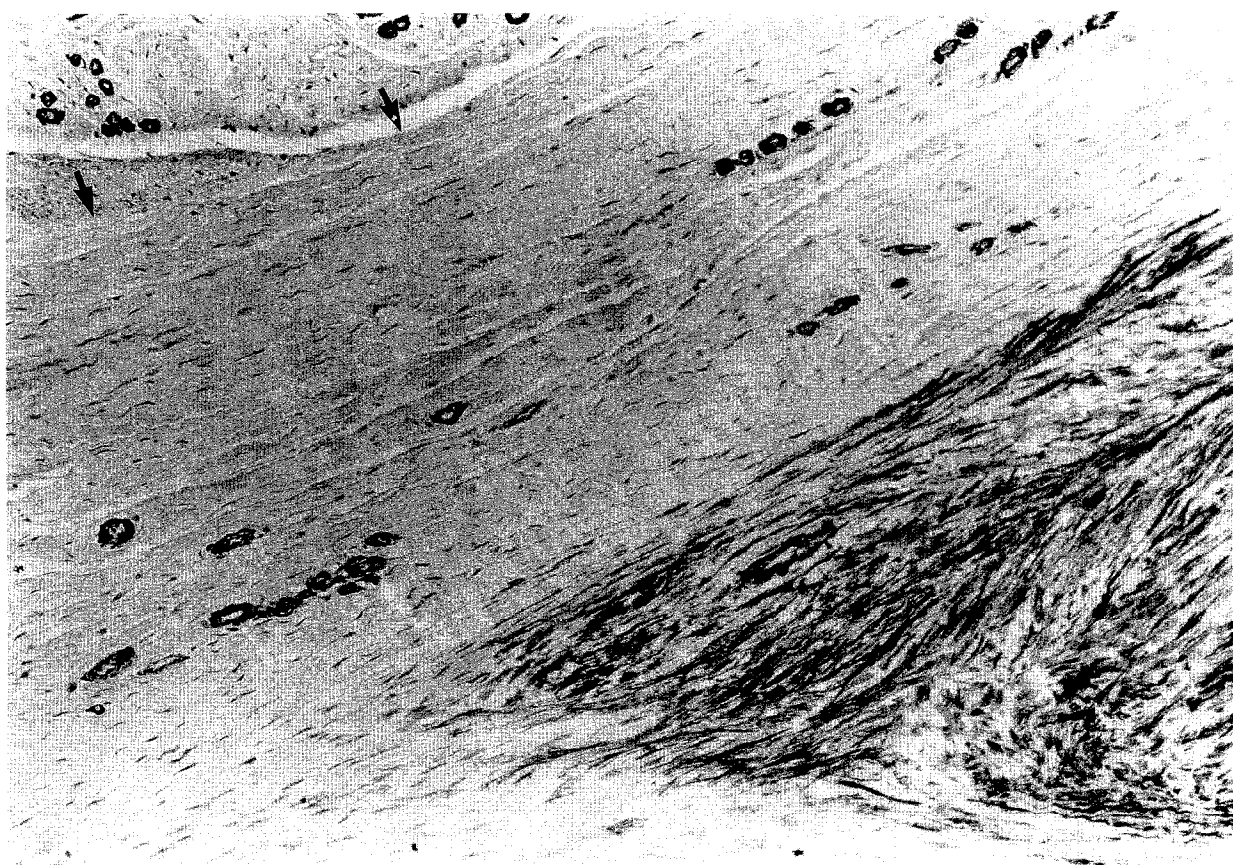


Fig 1 Dupuytren's contracture fills the field. The bottom right shows cellular tissue staining for SM α -actin. The broad diagonal band running from the top to bottom (poorly cellular Dupuytren's tissue) does not stain. Blood vessels stain positively. SM α -actin $\times 125$ Immunoperoxidase.

METHODS

Samples of Dupuytren's cord with overlying clinically involved skin were taken from 20 patients undergoing dermofasciectomy for Dupuytren's flexion contracture.

17 of the patients were undergoing surgery for primary disease and three for recurrent disease. 15 were male and five female with an age range from 47 to 81 years. Approximately 2×2 cm of skin was taken with an underlying block of cord and subcutaneous tissue.

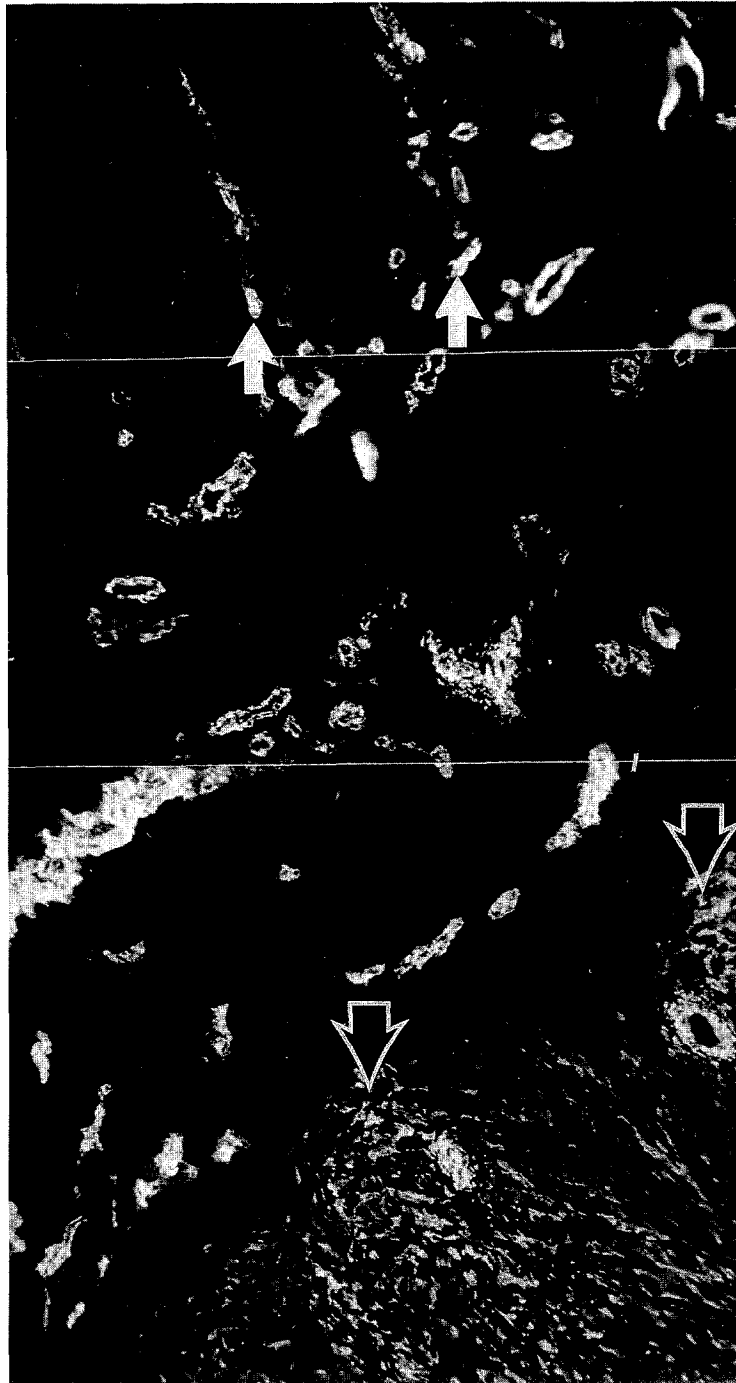


Fig 2 Skin montage showing hypercellular Dupuytren's within the lower dermis. The rete ridges are outlined by loops of positive staining vessels (solid arrows). Cellular tissue staining for SM α -actin seen at the bottom (open arrows). Immunofluorescence $\times 160$.

Orientation was maintained and the samples divided transversely, half for wax embedding and half for quick freezing in liquid nitrogen.

Specimens for light microscopy were fixed in formalin and embedded in paraffin wax in the routine manner. Sections were stained with haematoxylin and eosin and with antibody against SM α -actin (Dakopatts) using the avidin-biotin complex (ABC) immunoperoxidase technique (Hsu et al, 1981). Quick frozen samples were stored at -70° until sectioned on a cryostat at $4\ \mu\text{m}$. Sections were immediately post-fixed in formal-acetic acid-alcohol and air dried. Subsequent staining for immunofluorescence microscopy was as described in Skalli et al (1989). The antibody used in both methods was the same (Skalli et al, 1986). The nuclei were stained with DAPI (Boehringer Mannheim UK, Lewes) at a concentration of $\mu\text{g/ml}$ for ten minutes at 25° .

RESULTS

In the material from 15 of the 20 patients (11 male, four female), varying amounts of expansile, hypercellular, collagenous tissue were identified. The Dupuytren's tissue of the remaining five patients was made up entirely of largely acellular cords. Within the hypercellular foci

the degree of cellularity was very variable and changed from highly cellular to much less cellular, even within individual sections (Figs 1 and 2). The cell nuclei of the hypercellular regions were always swollen and rounded, in marked contrast to the largely acellular regions which were characterized by very elongated thin nuclei. All samples with hypercellular foci stained for SM α -actin. The patterns seen varied from very intensely staining foci to weakly staining rather dispersed patches. In general the more cellular a patch of tissue, the stronger the stain for SM α -actin. Both wax embedded, immunoperoxidase stained sections and cryostat cut material examined by immunofluorescence microscopy gave the same positive identifications. In the negative samples only staining of the smooth muscle cells within the blood vessel walls was observed.

In 15 cases, the Dupuytren's tissue extended into the dermis (Fig 3). 12 of these were hypercellular and stained for SM α -actin. Three consisted only of rather acellular collagenous tissue which failed to stain for SM α -actin. The extent of dermal infiltration was variable: in some only the lower dermis was involved (Fig 2) but in three cases the Dupuytren's tissue actually reached the base of the epidermis (Fig 4).

In addition to the presence of compact Dupuytren's

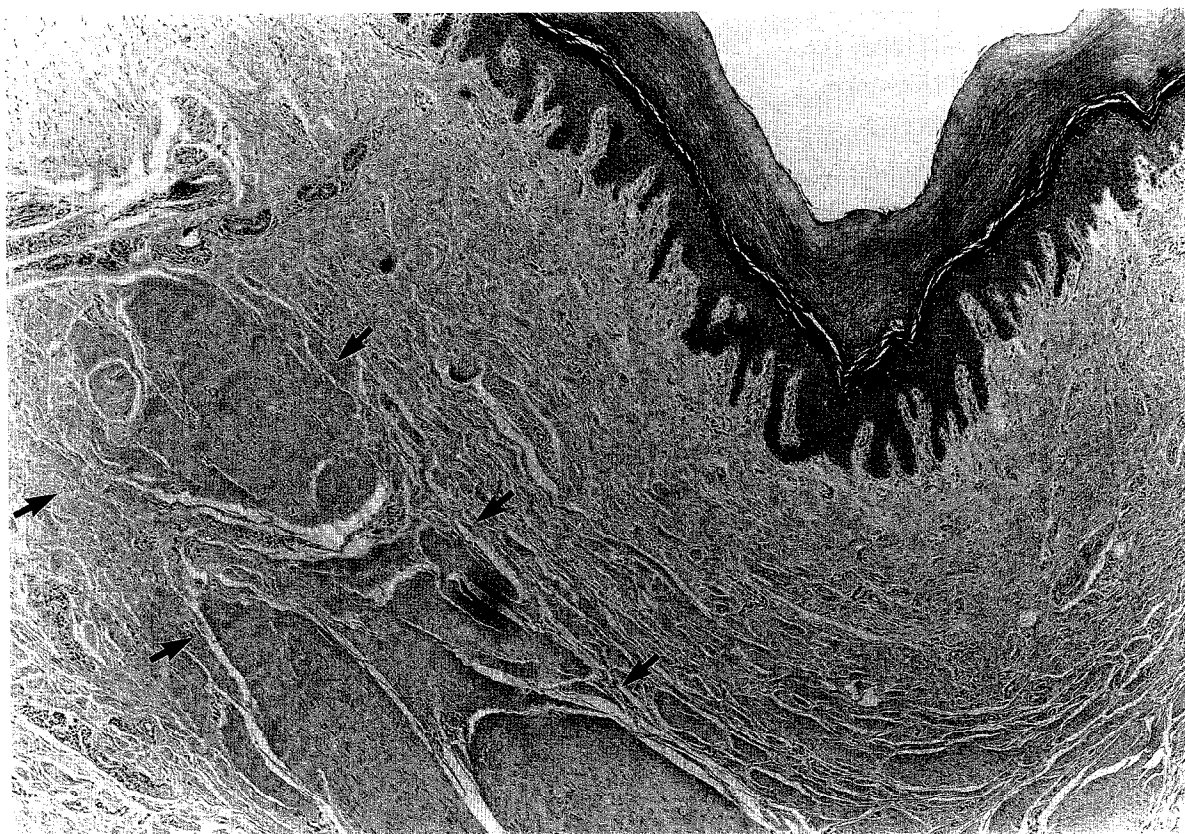


Fig 3 Infiltration of dermis (subcutis not included) by Dupuytren's tissues (arrows). The skin is retracted. HE $\times 50$.

tissue in the dermis, eight samples showed the presence of a diffuse increase in fibroblasts which also stained for SM α -actin (Fig 5). These cells were distributed singly in the upper dermis, in some cases remote from the main lesion, and there was no gradient of cell density to suggest "fade out" of the infiltrating Dupuytren's lesion. Generally, samples showing cellular hypercellular Dupuytren's tissue also contained dispersed SM α -actin positive fibroblasts. In one patient, however, the dispersed fibroblasts were associated with an acellular Dupuytren's lesion.

DISCUSSION

Two techniques have been employed to investigate the presence of SM α -actin positive cells: immunoperoxidase staining of paraffin embedded material and immunofluorescence staining of cryostat cut material. In general there was a very good agreement between the two methods. In all cases the cells within hypercellular foci stained positively for SM α -actin using both methods. The immunoperoxidase technique was found to be superior in demonstrating the distribution of the SM α -actin cells. Although the Dupuytren's "nodules" were well delineated by immunofluorescence it was not

always possible to determine the location of individual SM α -actin positive cells against background staining.

Our results confirm the findings of Skalli et al (1989) that the characteristic myofibroblasts of Dupuytren's fibromatosis stain strongly with antibodies against SM α -actin and that this antibody is a good marker for the hypercellular phase of the disease. This hypercellular tissue was usually also associated with largely acellular "cord" material, which showed only weak staining. This is in accord with the findings of Luck (1959) and Chiu and McFarlane (1978), who described the "nodule-cord" as a common entity in the involuntional phase of the disease, with one type of structure merging into the other, rather than a sharp separation. In this series, myofibroblast rich foci were seen not just in the subcutis but also in the dermis, in three cases running right up to the epidermis itself. Contracture tissue has been previously recorded to involve the skin frequently, and myofibroblasts have been identified within the dermis using electron microscopy (Vande Berg et al, 1982). These authors found myofibroblasts only in the lower dermis but the present findings demonstrate that such tissue can extend right up to the epidermal boundary.

In addition, dispersed populations of fibroblasts, also staining for the presence of SM α -actin, were found in

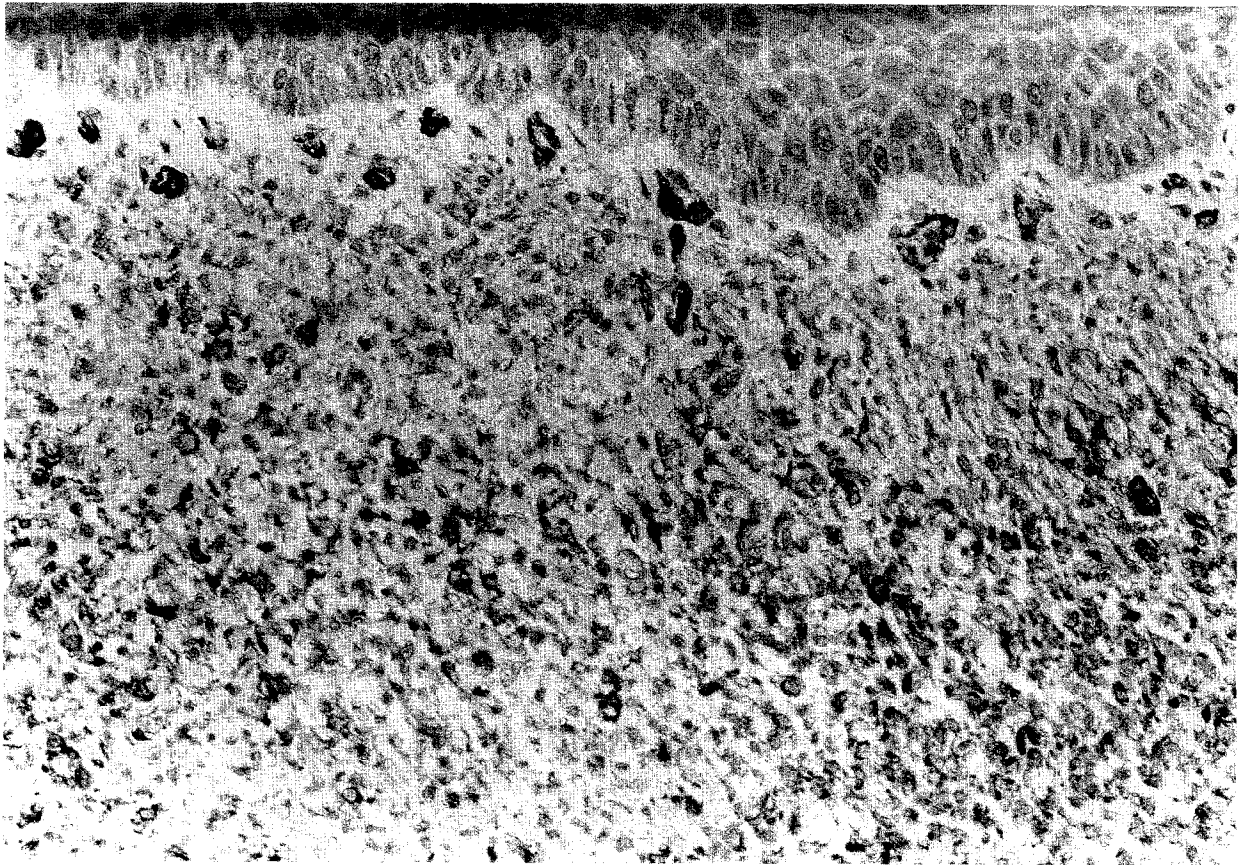


Fig 4 Dupuytren's tissue reaching epidermis. SM α -actin \times 250 Immunoperoxidase.

the subcutis and dermis in eight out of the 20 samples. These fibroblasts were separate from the hypercellular Dupuytren's lesion and were frequently situated at some distance from the borders of the lesion. Such cells have not previously been recognised. Gabbiani and Majno (1972) originally proposed that the myofibroblasts form-

ing the hypercellular foci initiated the contracture. We further hypothesize that the isolated SM α -actin positive fibroblasts may provide a pool of progenitor cells from which the foci may develop.

It has been found that replacement of the volar skin with a full thickness graft prevents recurrence of

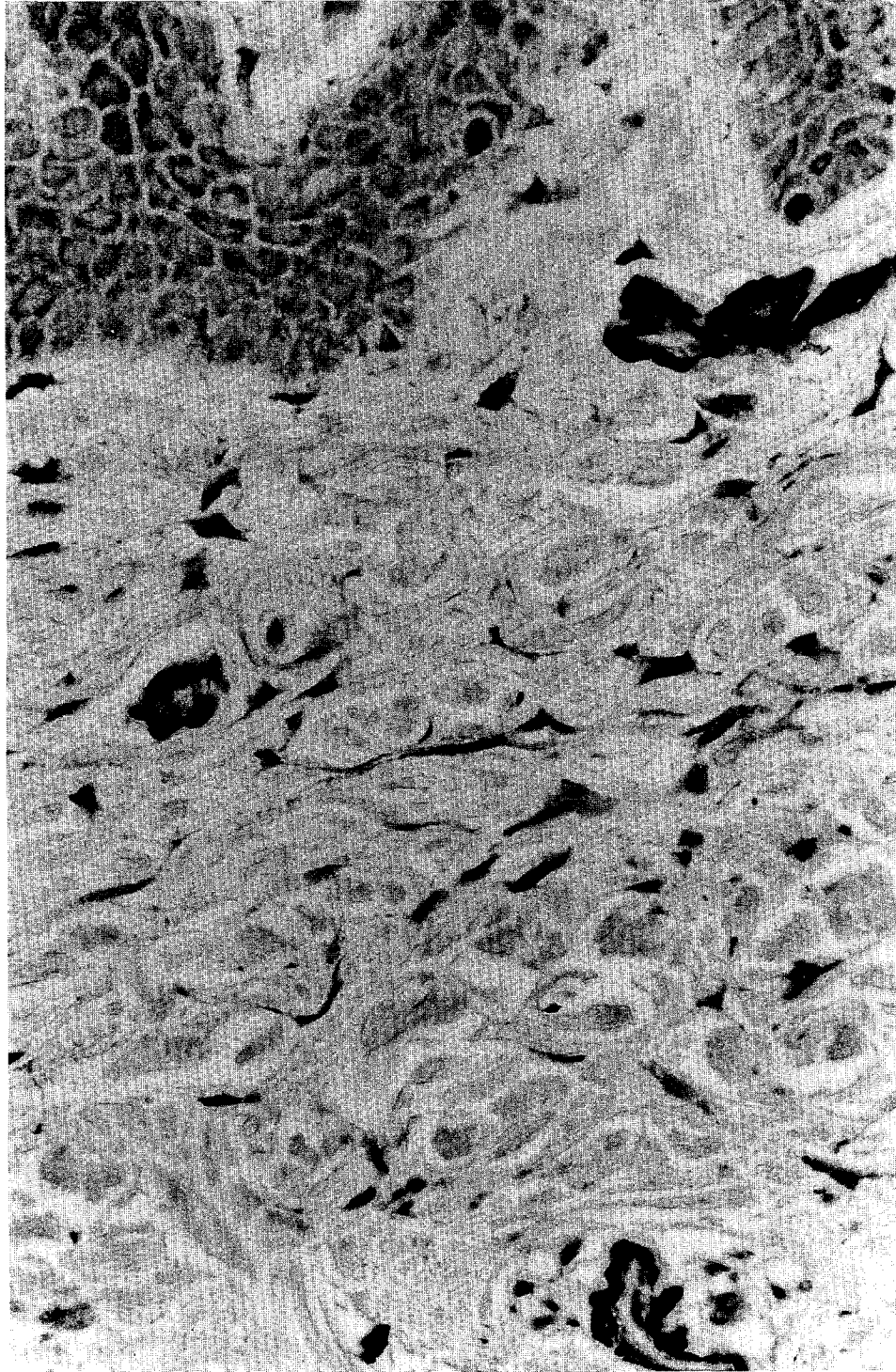


Fig 5 Scattered SM α -actin positive cells in the upper dermis. SM α -actin $\times 500$ Immunoperoxidase.

Dupuytren's contracture (Hueston, 1962; 1969; 1975). Our findings of both hyperproliferative Dupuytren's foci and also isolated SM α -actin positive fibroblasts in the dermis provide a possible explanation of the source of the recurrence. It may be due to expansion of already active foci, or alternatively to activation of quiescent progenitors. Gelberman et al (1980) found a correlation between the presence of myofibroblasts (as identified by electron microscopy) in Dupuytren's foci removed at operation and recurrence of the disease.

Acknowledgements

Financial support by the East Anglian Regional Health Authority to carry out this research is gratefully acknowledged. We would also like to thank Karen Turner for typing this paper.

References

- CHIUI, H. F. and MCFARLANE, R. M. (1978). Pathogenesis of Dupuytren's contracture: A correlative clinical-pathological study. *Journal of Hand Surgery* 3: 1: 1-10.
- GABBIANI, G. and MAJNO, G. (1972). Dupuytren's contracture: Fibroblast contraction? An ultrastructural study. *American Journal of Pathology*, 66: 1: 131-146.
- GELBERMAN, R. H., AMEIL, D., RUDOLPH, R. M. and VANCE, R. M. (1980). Dupuytren's contracture: An electron microscopic, biochemical and clinical correlative study. *Journal of Bone and Joint Surgery*, 62A: 425-232.
- HUESTON, J. T. (1962). Digital Wolfe grafts in recurrent Dupuytren's contracture. *Plastic and Reconstructive Surgery*, 29: 342-344.
- HUESTON, J. T. (1969). The control of recurrent Dupuytren's contracture by skin replacement. *British Journal of Plastic Surgery*, 22: 152-156.
- HUESTON, J. T. (1975). Dupuytren's contracture: Selection for surgery. *British Journal of Hospital Medicine*, 13: 361-370.
- HSU, S. M., RAINE, L. and FANGER, H. (1981). The use of antiavidin antibody and avidin-biotin-peroxidase complex in immunoperoxidase technique. *American Journal of Clinical Pathology*, 75: 6: 816-821.
- LUCK, J. V. (1959). Dupuytren's contracture: A new concept for the pathogenesis correlated with surgical management. *Journal of Bone and Joint Surgery* 41A: 4: 635-664.
- MCGROUTHER, D. A. Recurrence and Extension. In: McFarlane, R. M., McGrouther, D. A. and Flint, M. H. (Eds.): *Dupuytren's Disease*. London, Churchill Livingstone, 1990: 383-386.
- SCHÜRCH, W., SKALLI, O. and GABBIANI, G. The Myofibroblast. Definition, Ultrastructural Features and Role in Wound Contraction. In: McFarlane, R. M., McGrouther, D. A. and Flint, M. H. (Eds.): *Dupuytren's Disease*. London, Churchill Livingstone, 1990: 31-47.
- SKALLI, O., ROPRAZ, P., TRZECIAK, A., BENZONANA, G., GILLESSEN, D. and GABBIANI, G. (1986). A monoclonal antibody against α -smooth muscle actin: A new probe for smooth muscle differentiation. *Journal of Cell Biology*, 103: 6(2): 2782-2796.
- SKALLI, O., SCHÜRCH, W., SEEMAYER, T., LAGACÉ, R., MONTANDON, D., PITTET, B. and GABBIANI, G. (1989). Myofibroblasts from diverse pathologic settings are heterogeneous in their content of actin isoforms and intermediate filament proteins. *Laboratory Investigation*, 60: 2: 275-285.
- VANDEBERG, J. S., RUDOLPH, R., GELBERMAN, R. and WOODWARD, M. R. (1982). Ultrastructural relationship of skin to nodule and cord in Dupuytren's contracture. *Plastic and Reconstructive Surgery*, 69: 5: 835-844.

Accepted: 22 April 1993

Dr B. G. McCann, Histopathology Department, Norfolk and Norwich Hospital, Brunswick Road, Norwich, NR1 3SR, UK.

© 1993 The British Society for Surgery of the Hand