

occurred in either group, there were four reported hematomas in the closed-palm group which resulted in prolonged wound healing in each case, and in one case, full-thickness skin loss in the palm required subsequent skin grafting. Consideration must also be given to the possible influence of undetected hematoma and persistent edema in potentiating postoperative scar formation and thereby limiting ROM. The open-palm technique may, therefore, be most applicable for patients with extensive disease if leaving the palmar wound open would avoid wound closure under tension and ensure adequate blood supply to the wound margin. The open wound also prevents hematoma formation in the palm and immediately permits increased MP extension.

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Microvascular changes in Dupuytren's contracture

Previous studies of certain fibrotic lesions (hypertrophic scar, keloid, pseudotendon) have revealed pervasive microvascular occlusion. Lowered oxygen tension is considered to be a stimulus to excessive collagen production and, hence, the scar. Because its characteristics are similar to those of other lesions, Dupuytren's contracture appeared to be a good model in which to confirm the presence of occluded microvessels. Six cases were examined by light, electron, and polarizing microscopy. Most of the microvessels from the precontracture band area throughout the periphery of the body of the nodules were occluded by a bulging of the endothelial cells into the lumen. The microvessels were surrounded by extensive layers of basal laminae. The nodules were essentially avascular. The presence of another fibrotic lesion in which pervasive microvascular occlusion occurs is suggestive of an underlying biologic principle concerning the generation of all fibrotic lesions. (*J HAND SURG* 9A:58-62, 1984.)

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Dupuytren's contracture is a fibrotic disease of the palmodigital aponeurosis in man in which the highly oriented collagenous matrix enlarges to form nodules and laminated bands. The etiology of this affliction is unknown, although several theories have been suggested concerning its origin and numerous important observations made concerning its pathogene-



Fig. 1. A typical microvessel, 3 μ m in diameter, from the peripheral vascular net about the body of the nodules. The lumen is occluded, and there are extreme layers of basal laminae (*L*), endothelial cells (*E*), and pericytes (*P*). (Magnification $\times 12,000$.)

sis.¹ Racial-genetic factors, trauma, alcoholism, diabetes mellitus, and arthritis, among others, have been cited by Krebs² and reviewed by Hueston.³ Although not a recognized naturally occurring disease in animals, a lesion typical of Dupuytren's contracture was produced experimentally in monkeys by Larsen et al.⁴ by traumatic rupture of the fascial fibers. Support for a role of mechanical factors in the pathogenesis of Dupuytren's contracture is derived from the observation of Skoog⁵ and confirmed by our experience in that the disease selectively involves those collagen fiber groups that are oriented longitudinally in the palmar aponeurosis. The contiguous transverse fibers of the palm are spared in this disease.

The contraction process in Dupuytren's disease has been related to the finding of myofibroblasts within the nodules.⁶⁻⁹ If this characteristic cell of repair and granulation tissue causes both the contraction and increase in collagen, it is not clear why it should be present in the absence of an open wound.

It is interesting to note that Hueston^{1, 3} and others remarked about vascular disturbances as a possible factor in Dupuytren's contracture and commented on the

need for studies of the vascular pattern of normal and diseased palmar tissues. Hueston¹⁰ states, "It has certainly not been possible to verify the claim of Davis¹¹ [our reference] that there is an abnormality of the ulnar artery in every hand of Dupuytren's contracture . . . whatever is . . . found to be responsible for the anatomical or physiological vascular abnormality will then be the cause of Dupuytren's contracture." Nezelof¹² cites hypervascularization of Dupuytren's lesion and identifies venous stasis as being present.

Previous studies of hypertrophic scars and keloids¹³⁻¹⁵ and of wounds of deep injuries by Kischer¹⁶ have examined the role of microvascular occlusion (and probable diffusion deficits) in the generation of these lesions. These studies suggested a general hypothesis relating the pathogenesis of fibrotic disease to microvascular occlusion and hence to hypoxia-stimulated collagen excess. Therefore, we predicted we would find occluded microvessels in Dupuytren's contracture.

Method and materials

Fresh tissues from six patients with Dupuytren's contracture were obtained after surgery, pinned to a

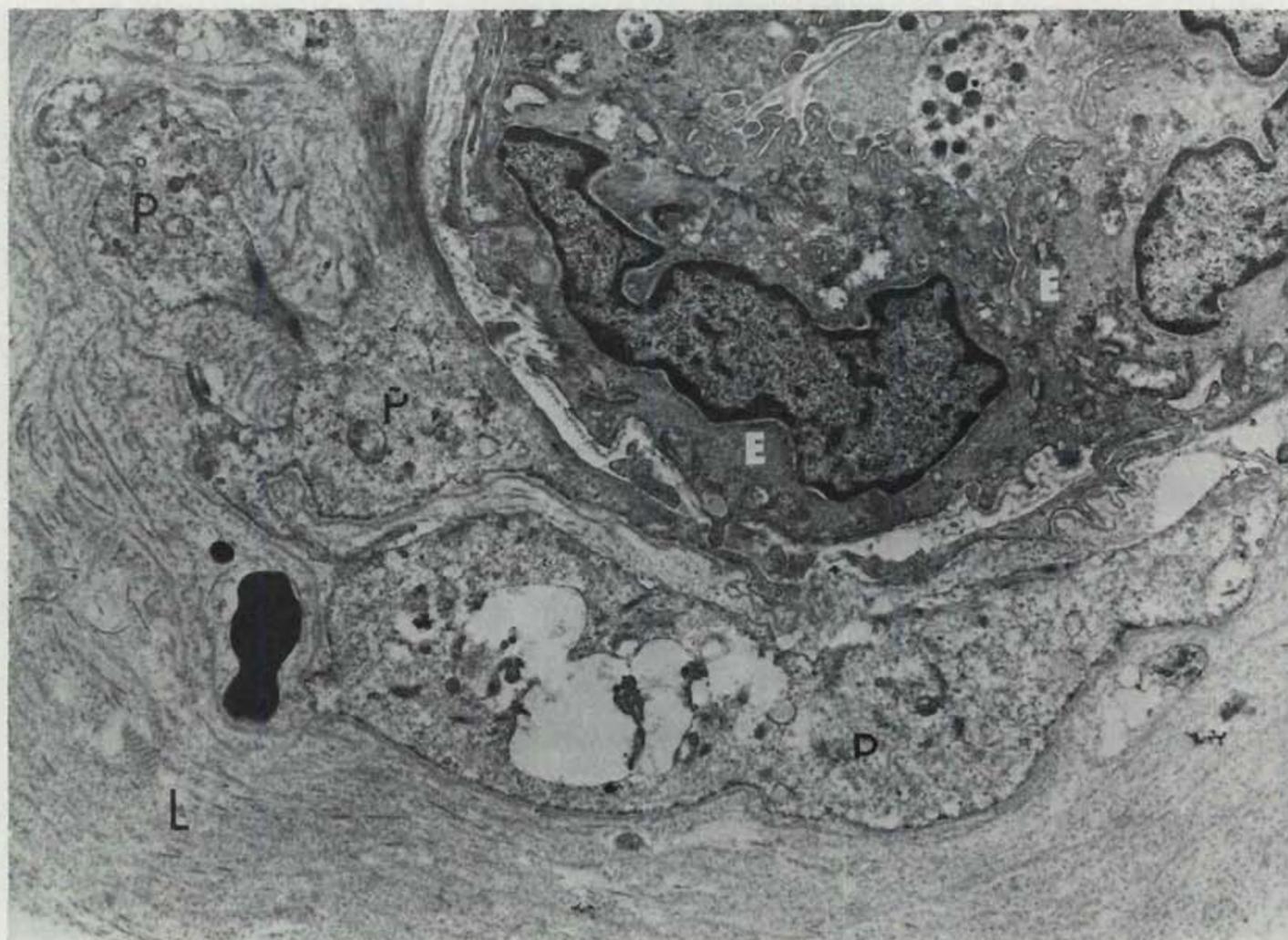


Fig. 2. Microvessel, 10 μm in diameter, from preband (prenodular) area. Small, partially occluded lumen, 4.5 μm in diameter, and multilayering of basal laminae (L), endothelial cells (E), and pericytes (P). (Magnification $\times 8000$.)

tongue blade to maintain alignment and length, and immediately placed in Karnovsky's fixative. Of these patients, one was an insulin-dependent diabetic, none recounted a specific trauma to the palm although all had at some time performed some degree of manual labor, one had a long exposure to industrial solvents of several kinds, and while all used alcoholic beverages, only one was alcoholic and suffered from overt hepatic disease. Two of the patients had combined flexion contracture of the metacarpophalangeal and proximal interphalangeal joints of one or more fingers that exceeded 90° . The remainder had contractures greater than 30° that had evolved over periods of less than 2 years preoperatively. Total excision of the involved palmar aponeurosis was carried out by means of sharp dissection with thin regions of adjacent fatty tissue preserved with the specimens.

Whole sections, both longitudinal and transverse, of the nodule, proximal and distal areas, and prenodular tissue were obtained by razor blade cuts. Adjacent pieces were processed through paraffin for light microscopy study and for examination by electron microscopy. Light microscopy sections were stained with

hematoxylin-eosin, Masson's trichrome and periodic acid-Schiff (PAS). Tissues selected for studies by transmission electron microscopy were dissected into small pieces approximately 3 mm^3 . After washing with isotonic cacodylate buffer the tissues were postfixated for 1 hour in 1% OsO_4 with cacodylate buffer. After another buffer wash, the tissues were dehydrated through graded alcohols and embedded in Epon 812. Sections were cut with a diamond knife, stained with uranyl acetate, and examined in a Philips 300 electron microscope. For the electron microscopy studies, care was taken to include the perinodular microvascular net including some fatty tissue.

Specimens were also studied by polarized light microscopy to confirm the orientation of the collagen fiber systems in the pathological tissue.

Results

In all of the six cases, electron microscopy showed most of the sections, from prenodular to perinodular including proximal and distal portions, to have microvessels with occluded lumina and a tremendous increase and excessive layering of the basal laminae

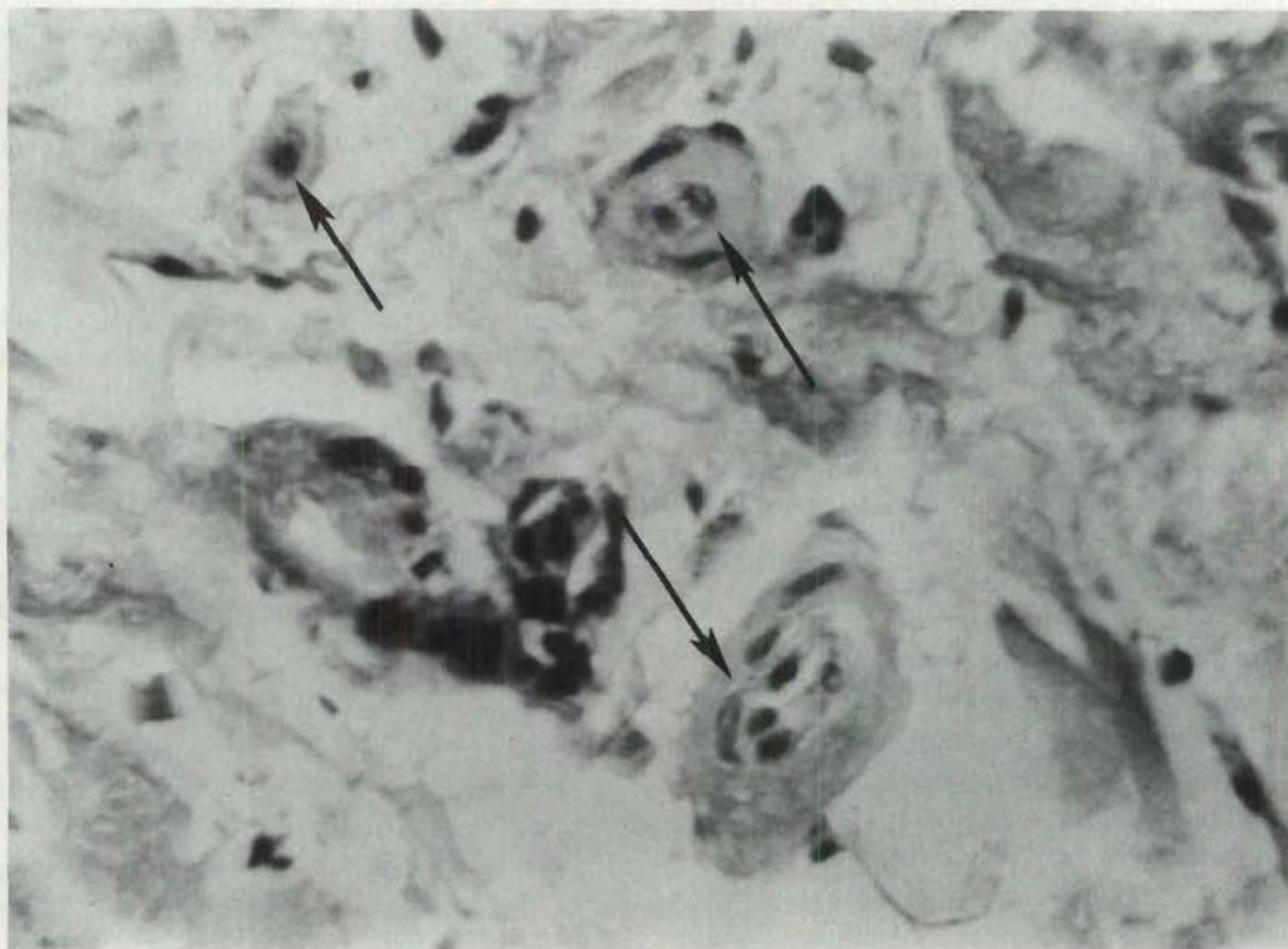


Fig. 3. Set of microvessels from periphery of nodules. Two have occluded lumina and one has a partially occluded lumen. All three have extensive basal laminae (\rightarrow). Paraffin section stained with Masson's trichrome method. (Magnification $\times 500$.)

(Figs. 1 and 2). The occlusion of the microvessels appears to be caused by an increase in the number of endothelial cell profiles, usually up to four or five (normal number is one or two), so that they bulge into the lumen. All of the microvessels are surrounded by pericytes, often several of them. The bulk of the microvessels are oriented parallel to the long axis of the contracture band. The trichrome and PAS-stained sections demonstrate the occluded microvessels with the increased amount of basal laminae (Fig. 3), but this condition of the microvessels is not so easily recognized by hematoxylin-eosin staining. In all six cases most of the sections studied by transmission electron microscopy contained myofibroblasts.

Polarized light microscopy of band tissue shows that the predominant orientation of collagen fibers is in the longitudinal axis of the band.

Discussion

Occluded microvessels are consistently present, not only about the contracture bands and nodules but around the prenodular areas as well. How far these vessels are occluded proximal or distal to the bands

proper is unknown for we have made studies through prenodular distances of only 5 to 10 mm.

The number of concentric basal lamina layers was surprisingly large and was even more extensive than that observed in cases of diabetes mellitus. Yodaiken¹⁷ indicates that this thickening by layering of basal laminae is related to hypoxia, which would be consistent with our findings in hypertrophic scars and keloids and would tend to support our contention that hypoxia stimulates collagen production.¹³

There is also some evidence that the basal laminae may be regenerated by pericytes and that the number of rings of basal laminae about the endothelium may be correlated with the number of pericyte cell generations occurring at that site.¹⁸ In the cases of Dupuytren's contracture reported herein, there are multiple layers of pericytes. This feature is also seen in granulation tissue¹⁶ and in some hypertrophic scars.¹³⁻¹⁵

Sobin et al.¹⁹ and Bernick et al.²⁰ have described microvessels with age-related changes of increased periendothelial PAS staining. Although no electron microscopy was done in these studies, it seems certain this represents an increase in basal laminae. This con-

dition has implications relative to diffusion capability and hypoxia.

The myofibroblast is the principal cell in the pathogenesis of the Dupuytren's contracture band, but the inductive and cellular origin of the myofibroblast is not established. It is suggested that hypoxia, caused by luminal occlusion from excessive numbers of endothelial cells, will stimulate the pericyte to differentiate to a myofibroblast. This sequence has been supported by an extensive study of hypertrophic scars and keloids.¹⁵ This scheme suggests the origin of the lesions begins with some stimulus, perhaps trauma, to endothelial cells that increases their number, vascular branching, and pericyte members. With a subsequent increase in myofibroblasts and collagen, the pattern for fibrosis is established.

The finding of a second fibrotic lesion with pervasive microvascular occlusion, excessive pericytes, fibroblasts, and basal laminae may suggest a general pathogenetic phenomenon for fibrotic disease. Such a hypothesis is particularly attractive in the case of Dupuytren's contracture for it places the microvascular phenomenon as a common pathway through which trauma, diabetes (microangiopathy), hereditary variations in vascular pattern, and alcoholism (hepatic disease) may produce a similar fibrotic palmar lesion.

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