DUPUYTREN'S CONTRACTURE II—SCANNING ELECTRON MICROSCOPIC OBSERVATIONS

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INTRODUCTION

The scanning electron microscope (SEM) is an extremely versatile instrument which combines a great depth of focus (three hundred times that of a light microscope) with fairly high resolution (15 nm) to give a three-dimensional image of the surface of a specimen. Because of these properties, it is particularly suitable for studying the organisation of a tissue. By applying it to samples of Dupuytren's contracture, we have been able to clarify some important details of the progression of this condition.

MATERIALS AND METHODS

Seven Dupuytren's contractures and 5 normal palmar fascias were fixed in formol saline pH 7.0, frozen in "Arcton 12" and sectioned in various planes. Thick (100 μm) sections were prepared for SEM by the method of Finlay and Hunter (1971) while corresponding thin (7 μm) sections were stained by haemotoxylin and eosin, mounted and examined in the light microscope.

RESULTS

Normal Palmar Fascia. In the area of the fascia selected for examination (the distal palm) the fascia consisted of flat, interweaving fibres held together by a fine feltwork of fibrils which generally did not fuse with the fibres (Fig. 1).

Dupuytren's Tissue. The fibrous organisation of the tissue varied with its maturity and the features described here have direct histological counterparts. Actively growing areas (Fig. 2 and 3) were characterised by their cellularity and by a meshwork of fibrils (polymeric collagen) which coalesced into discrete fibres only focally and separated again within a very short distance (Fig. 2). These fibres would be described histologically as "poorly formed". An important feature is that both the constituent fibrils (Fig. 3) and the fibres themselves (Fig. 2) only tended to be orientated in one direction, in contrast to the mature tissue (Figs. 4 and 5). The predominant cells were smooth and oval but a few large cells with indented surfaces were found also. Too much reliance should not be placed, however, on cellular morphology since the preparative procedures used were not designed for studying cells.

As the tissue matured, the fibres became more compact and lay more or less in one direction. The constituent fibrils were more uniformly orientated and the space be-
between the fibrils (and between the fibres) diminished. In the mature nodule and fibrous band, the fibres consisted of closely packed parallel fibrils (Fig. 5) and had a wavy appearance (Fig. 4) indistinguishable from tendon. At this stage, cells could be identified no longer.

In one sample, small foci of active tissue were found along the edge of, and in the substance of, an otherwise mature band. In this situation, the fibrils became orientated and compacted into mature fibres over a very short distance. Whether these constituted the growing points for that band or repair of microruptures is impossible to say.

**DISCUSSION**

In the previous paper (Hunter, Ogdon and Norris, 1975), we analysed the polymeric collagen fibrils of Dupuytren’s tissue and showed that maturation of these fibrils was associated with an increase in chemical cross-linking. In this paper we have shown that maturation of the tissue *in vivo* also involves changes in the orientation of the fibrils within fibres and fibre bundles.
This observation is of functional significance because the orientation of fibrils and fibres determines to a large extent the mechanical properties of the tissue (Gustavson, 1956). Direct mechanical measurements were not performed on the samples, but, by applying general principles derived from studies on structurally similar tissues, it is possible to make reasonable predictions of the mechanical properties of immature and mature Dupuytren’s tissue. The fibrils of immature tissue only tend to be orientated in one direction and since they (and indeed the poorly formed fibres) are separated by comparatively large amounts of ground substance, this tissue will probably have little tensile strength but considerable extensibility. Mature tissue, on the other hand, with its compact, uniformly orientated fibrils will presumably behave like tendon and have great tensile strength but little extensibility. Clinical contracture is, of course, a manifestation of this inextensibility of the mature tissue.

Our studies have also given some insight into the process of maturation, a subject on which remarkably little has been written. Hueston (1963) summarised the vagueness of
contemporary thought on this subject in the phrase "maturation with collagenisation leads to shrinkage". Our results indicate that this concept is too simplistic; it seems very unlikely that collagen fibres in the proliferative areas (Figs. 2 and 3) can "mature" to the tendinous structure seen in Figure 4 purely by the accretion of newly formed collagen fibrils although this is obviously an important factor. Nor can the change in organisation be accounted for by postulating only a realignment of the fibrils in the immature fibres in direct response to an applied force; for such a mechanism would tend to produce a fibrillar knot rather than the uniformly orientated fibrils of the mature fibre bundles. The most satisfactory explanation of the observed change in fibrillar organisation is that maturation of Dupuytren's tissue involves remodelling of the collagen, i.e. breakdown of some of the fibrils (and therefore molecules) and their replacement by new fibrils with a different orientation and organisation. The simultaneous remodelling of the ground substance (Hunter, Ogdon and Norris, 1975) probably also contributes to the observed changes in fibre structure.
The dynamic nature of these changes may help to explain the progression (though not the aetiology) of Dupuytren's contracture more satisfactorily than the classical static descriptions. The following concept is based on the general principle that the fibre (and fibril) orientations of connective tissues are living "diagram of the forces" acting on that tissue. The trabecular pattern of the neck of the femur is probably the best example of this law while the tendinous bands of Dupuytren's contracture itself have long been recognised as following the line of force passing from the palm into the finger. An important corollary of this thesis is that fibroblasts can sense an orientational stress and respond to it by laying down collagen along the resultant lines of force, thereby counteracting the initial stress. In this respect the fibroblasts of Dupuytren's contracture behave normally. Thus, if the fibrous architecture of any area of Dupuytren's tissue depends on the forces acting locally on the fibroblasts, it will be remodelled if the exogenous stress changes either in amount or direction. The application of this theory is best illustrated by examples. Consider the following two clinical presentations:
A single small focus of fibroplasia in the areolar tissues of the palm. This exhibits considerable variation in fibrill orientation and packing density, since it is acted on by a multitude of weak forces acting via the fibrous septa within the fat. However, when the disease process spreads to join dermis to aponeurosis, the strains produced in these tissues by normal hand movements act on the Dupuytren's tissue which is remodelled to cope with these stresses and may contract. Contraction is an active process due partly to the changing pattern of fibril and fibre orientation but also to fibroblast movement, cell contact and activation of intracellular contractile elements (Gabbiani and Majno, 1972). The combination of active cell mediated contraction and passive contracture due to the inextensibility of the highly orientated replacement fibrils and fibres produces secondary changes in the dermis and aponeurosis. A cycle is thus set up which ceases only when the forces balance. The resulting clinical features may range from a small dermal dimple to widespread changes depending on the area involved.
The classical contracture which develops when the disease process joins inextensible tissue across a joint. The fibrous tissue laid down initially is fairly extensible and relaxed even when the fingers are extended. Collagen laid down subsequently with the finger flexed (i.e. the position of rest in which the hand remains for most of the day) is brought under tension when the finger is extended. With normal repetitive movements of the hand over a period of time, remodelling and contraction occur and the highly orientated replacement collagen acts as a block to full extension. This cycle is repeated and the deformity increases, particularly if an extrinsic force is applied to try to straighten the finger. There may, once again, be secondary changes ("work hypertrophy") in adjacent tissues not directly involved, but acted on, by the Dupuytren's tissue; for example the retinacula of the palmar aponeurosis.

The variations in clinical presentation of Dupuytren's contracture are protean and cannot all be considered here but the progression of all the lesions can be explained by the above concept. We must emphasise that it does not try to explain the aetiology of Dupuytren's disease. The immediate stimulus to fibroplasia in genetically susceptible individuals (Ling, 1963) is uncertain, but it is this factor which determines the location of, and therefore the dysfunction produced by, the disease. Once differentiated, however, the fibroblasts behave normally; their extracellular products are not chemically different from those of comparable connective tissues such as healing wounds and tendons (Hunter, Ogdon and Norris, 1975) and collagen fibrils are orientated correctly in relation to applied stresses. This normal cellular behaviour does not, of course, imply that Dupuytren's contracture is in any way physiological. Normal or "physiological" connective tissue are characterised by their precise adaptation to function. Dupuytren's tissue is pathological because it behaves as an adaptation which produces a malfunction.

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