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# The development of human digital tendons

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## INTRODUCTION

The development of tendons in human fetal specimens has been undertaken with special reference to the comparison between flexor and extensor tendons and possible factors controlling tendon differentiation. It has been found that the digital flexor tendon and its sheath is a complex 'organ' which develops in an orderly fashion from a solid core of cells, a process which is quite unlike that seen in repair after injury.

## MATERIALS AND METHODS

Eighteen fetal specimens from 40 days (approximately 20 mm crown–rump length (C.R.L.)) to 112 days (142 mm C.R.L.) post-coitum were obtained, processed and examined in this study.

Limb buds (or in older specimens, individual fingers) were placed directly into 4 % glutaraldehyde solution in phosphate buffer for up to 12 hours at 4 °C. Post-fixation was in 1 % osmic acid in 0·2 molar *s*-collidine buffer (pH 7·4) for 3–4 hours (4 °C). The specimens were dehydrated through alcohol solutions into propylene oxide and then embedded in epoxy resin (Luft, 1961). Polymerization was at 60 °C for 48 hours after vacuum embedding for 12 hours.

Thick sections (1 $\mu$m), obtained with a glass knife, were stained with Richardson's stain (Richardson, Jarrett & Fincke, 1960), for light microscopy. Thin sections (60–90 $\mu$m) for electron microscopy were cut with a diamond knife and stained with 1 % uranyl acetate at 60 °C for 30 minutes, followed by Millonig's lead stain (Millonig, 1961) for 30 seconds. The Associated Electrical Industries 6B model electron microscope was used.

## RESULTS

For descriptive purposes the specimens have been divided into groups according to their known gestation periods or their crown–rump lengths. Transverse and longitudinal sections were obtained in all cases.

### 20 *mm C.R.L.* (40 *days' gestation*)

*Light microscopy*

The flexor tendon (Fig. 1) is distinguishable as a condensation of cells within a general stroma of loose mesenchymal cells. Cells surrounding the tendon are

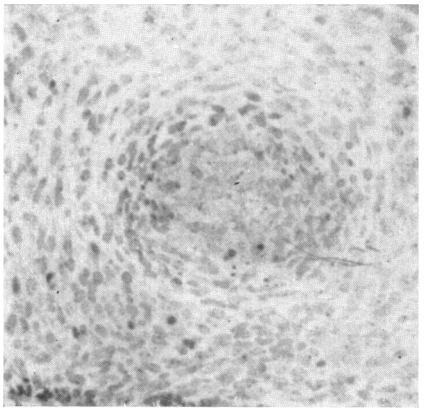

Fig. 1. Flexor tendon, 20 mm C.R.L. The tendon precursor is a condensation of cells within a loose stroma of mesenchymal cells. × 350.

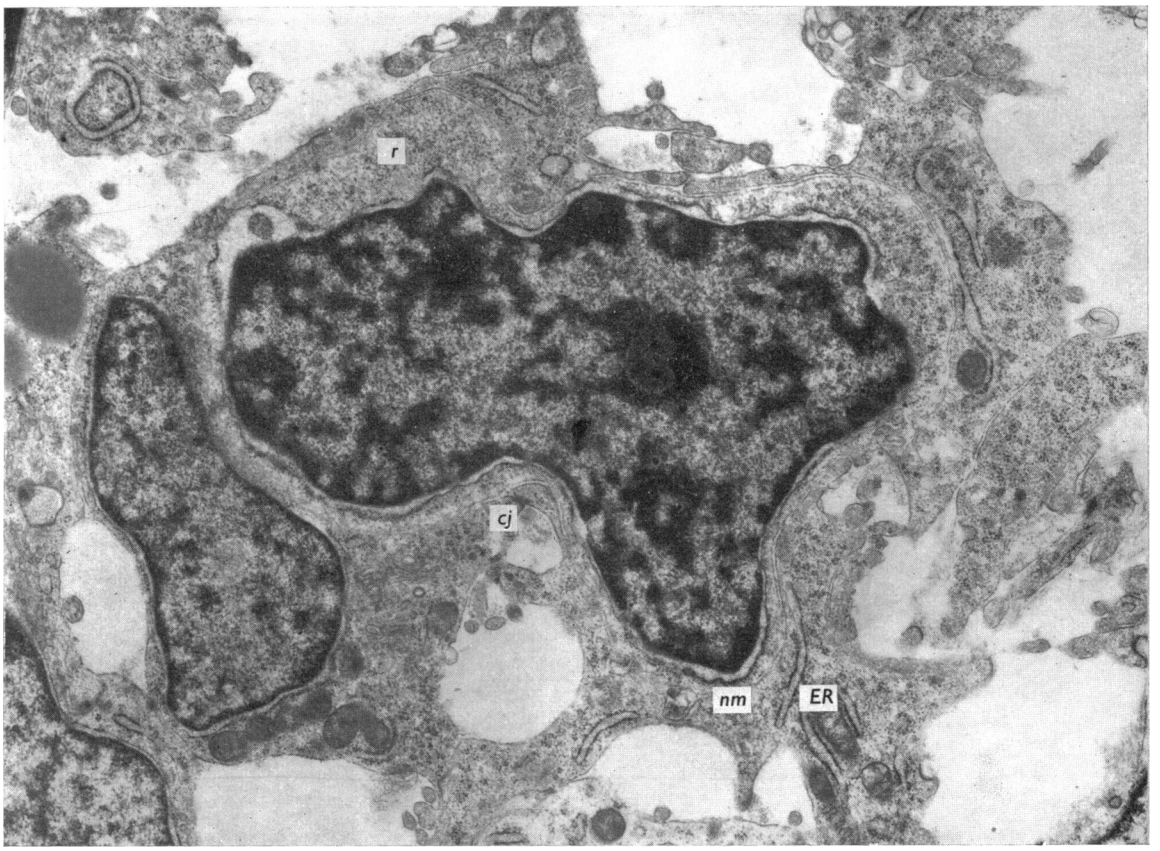


Fig. 2. Flexor tendon, 20 mm C.R.L. The cell shows close cellular apposition with occasional cell junctions (*cj*). The intercellular spaces are featureless except for fine fibrils close to the cell surface. The outer layer of nuclear membrane (*nm*) is separating and apparently forming endoplasmic reticulum (*ER*). Free ribosomes (*r*) are visible within the cytoplasm. × 15700.

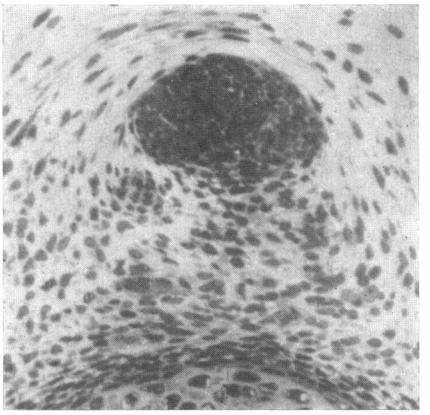

Fig. 3. Flexor tendon, 25 mm C.R.L. The tendon is now clearly demarcated from surrounding tissue. The primitive cartilage of the phalanx is seen inferiorly. × 350.

flattened circumferentially, but the boundary between tendon cells and general mesenchymal cells is not clear. The *extensor* tendon could not be identified in specimens at this age.

*Electron microscopy*

The flexor tendon cells are elongated with the long axis orientated along the length of the tendon. In places, the outer layer of the nuclear membrane (Fig. 2) shows separation from the nucleus itself and has local collections of ribosomes which represent the earliest stage in the development of endoplasmic reticulum. The cell cytoplasm contains occasional plaques of endoplasmic reticulum together with free single ribosomes and clumps of ribosomes. Infrequent mitochondria and a small amount of Golgi apparatus are visible.

Adjacent cells remain in contact with each other over broad areas of cell contact. At such sites the adjacent cell membranes are separated by a featureless gap of 30–50 nm. These areas of contact should be distinguished from specialized *junctional* areas, where the intercellular space becomes narrowed to 20nm and the adjacent cell cytoplasm stains densely. Cell junctions are a feature of many cell types, but in the developing tendon they will be seen to remain through differentiation, whilst the featureless areas of cell contact decrease, but do not entirely disappear, as the tendon develops. Larger intercellular spaces are now present but are featureless apart from a few villous cytoplasmic processes and irregular small fibrils close to the cell surface.

These electron microscopical features indicate that the tendon is producing protein to be utilized for cell growth (free individual and clumped ribosomes) whilst extracellular secretion of material has barely commenced (endoplasmic reticulum and mitochondria). Elongation of cells suggests that some force is already acting on the cell to induce a change in shape.

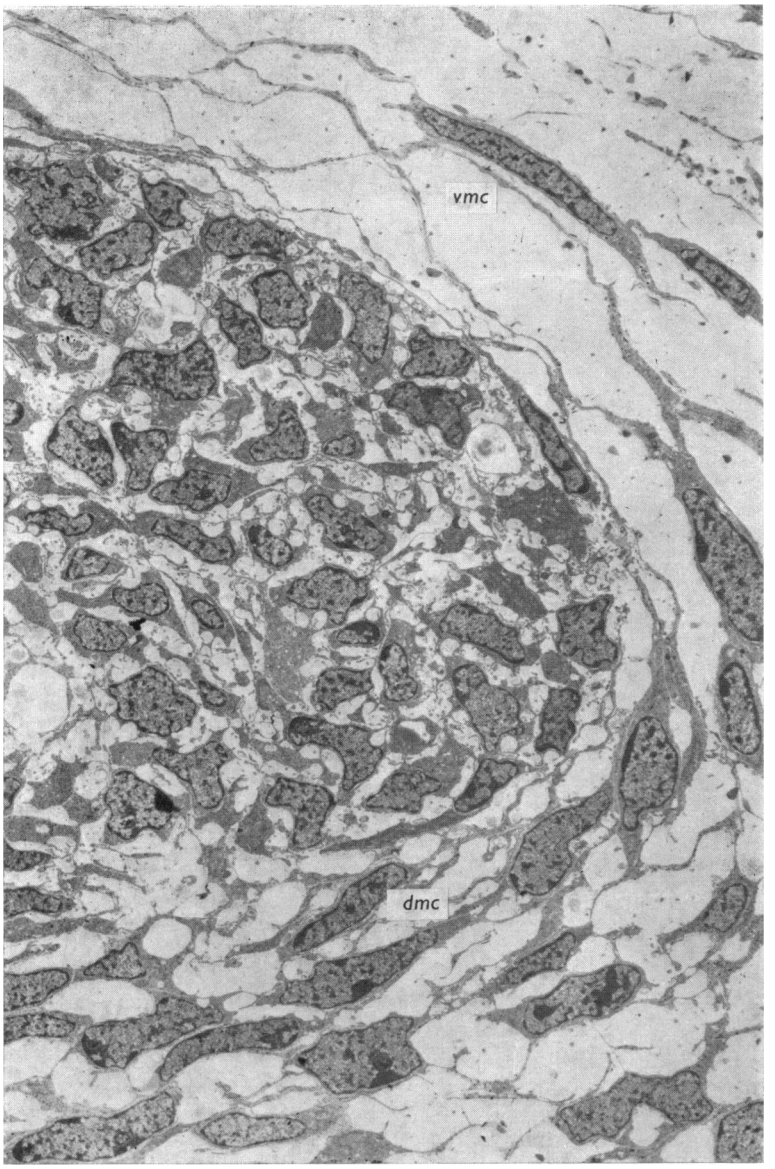


Fig. 4. Flexor tendon at 25 mm C.R.L. Ventral mesenchymal cells (*vmc*) are flattened and clearly distinguishable from cells of the tendon and the dorsal mesenchymal cells (*dmc*). × 2400.

### 25 *mm C.R.L.* (50 *days' gestation*)

*Light microscopy*

The flexor tendon cells (Fig. 3) remain closely packed and strongly basophilic and are clearly demarcated from the surrounding mesenchyme. Mesenchymal cells to the palmar side of the tendon are flattened, have little cytoplasm and are widely separated

from each other, whilst those on the dorsal (mesenteric or vincular) side of the tendon are rounded, have more cytoplasm and are more closely packed, although not as densely as the tendon cells.

The anlage of the *extensor* tendon is now identifiable as a layer of cells approximately four cells deep arranged around the primitive cartilage and separated from it by loose mesenchyme.

*Electron microscopy*

Each peripheral flattened mesenchymal cell (Fig. 4) demonstrates wafer thin cytoplasmic processes within an apparently structureless intercellular matrix. Some of these cells are closely applied to the tendon surface. On the dorsal side, the cytoplasmic processes are shorter and broader and the cells are thus closer together.

In the tendon itself the cells are more rounded and the nucleus occupies a large portion of the cell. The intercellular space and the number of fine collagen fibrils within the space have increased (seen at higher magnification), but the fibrils do not yet occupy the total available intercellular space.

A clear distinction already exists between those cells which will form tendon and those which will form sheath. The former are beginning to produce collagen fibrils with a definite longitudinal orientation, whilst the latter are relatively featureless.

40 *mm C.R.L.* (55 *days*)

*Light microscopy*

The *flexor tendon* is larger, and well differentiated from the surrounding mesenchyme and dorsal mesotendon. No synovial space has appeared. The *extensor tendon* (Fig. 5) is eight to ten cells thick and all the cells are flattened. Spaces are visible within the mesenchyme, both dorsal and ventral to the extensor tendon, but not closely related to the tendon itself, and may be considered similar to bursae, but are possibly artefactual.

*Electron microscopy*

The broad areas of cell contact seen in earlier specimens no longer exist (Fig. 6); rather, cells maintain contact by both small cytoplasmic processes (cell contacts) and specialized cell junctions which now have an intercellular distance of 25 nm (Fig. 7). Cell cytoplasm still contains some free individual and clumped ribosomes, but a more extensive endoplasmic reticulum has appeared and mitochondria are more numerous.

Cytoplasmic processes are abundant. The intercellular space is increased and appears to contain 'free' cytoplasmic fragments which in fact represent transverse section of villous processes. The collagen fibrils are extracellular and tend to lie in bays almost surrounded by cytoplasm (Fig. 8). Within these bays, collagen fibrils occupy all the available intercellular space, whilst at other points the intercellular space shows no fibril formation (Fig. 6). There are two sets of fibrils (Fig. 7): (1) Collagen fibrils averaging 29 nm in diameter and (2) bundles of much smaller fibrils (about 12 nm in diameter) which later appear to develop into elastic fibrils. The extensor tendon shows similar features, except that the individual cells are more flattened.

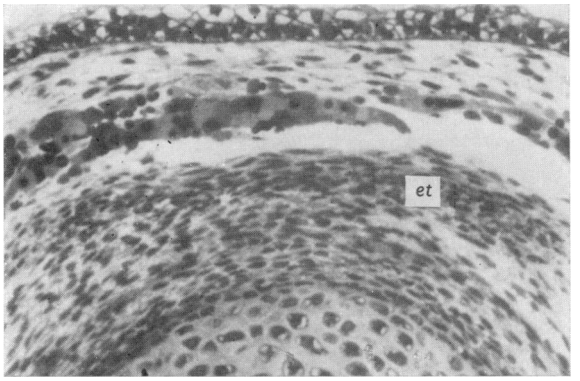


Fig. 5. Extensor tendon at 40 mm C.R.L. The extensor tendon (*et*) is a broad thin sheet arranged around the phalangeal cartilage. The space shown dorsal to the tendon represents a cleft in the surrounding mesenchyme. × 350.

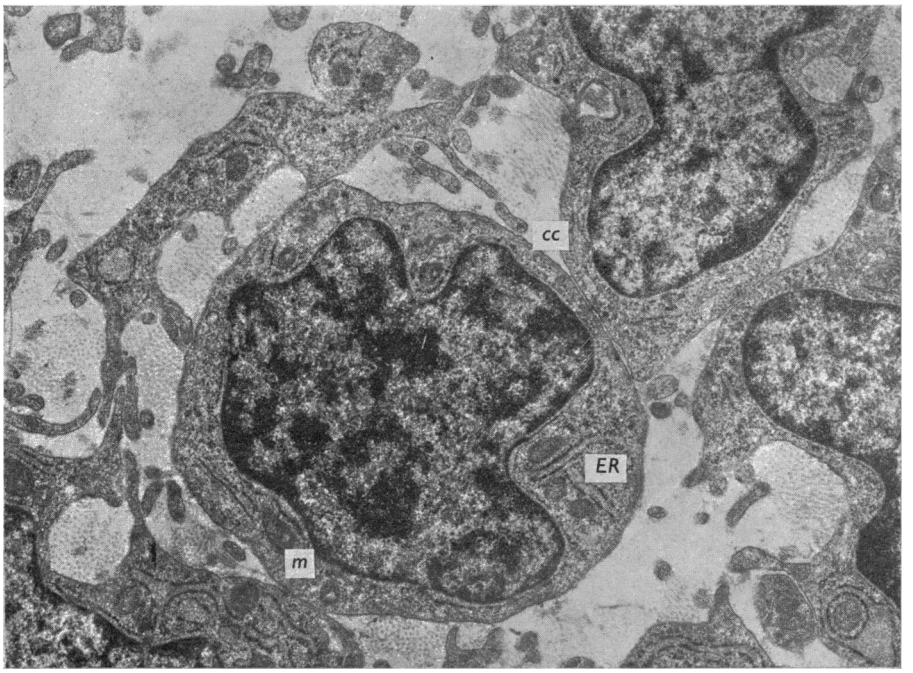


Fig. 6. Flexor tendon at 40 mm C.R.L. Individual cells are separating but remain attached by cell contact points (*cc*). Endoplasmic reticulum (*ER*) and mitochondria (*m*) are developing. × 17000.

The tendon cell at this stage shows the characteristics of a cell adapted to producing extracellular protein, as outlined by Rhodin (1967). Collagen fibrils of remarkably constant size are seen to be forming within bays of cytoplasm, but as yet, the collagen fibrils do not occupy the total available intercellular space.

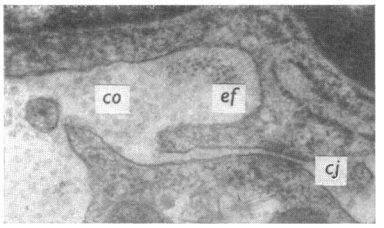


Fig. 7. Flexor tendon at 40 mm C.R.L. Two fibril types are demonstrated – collagen fibrils (*co*) and elastic fibrils (*ef*) within a cell 'nest'. A specialized cell junction site (*cj*) is also visible. × 32000.

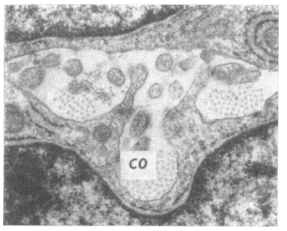


Fig. 8. Flexor tendon at 40 mm C.R.L. Early collagen fibril (*co*) deposition is within a 'nest' of cytoplasm. × 12600.

## 48 *mm C.R.L.* (60 *days*)

*Light microscopy*

A synovial space has now formed around the flexor tendon (Fig. 9). The space is crossed by a delicate reticulum of cells, most abundant in the mid-lateral areas. A single layer of cells is applied to the tendon – the visceral layer of synovium. In the specimen illustrated it can be seen that these cells are continuous with a mid-line septum within the tendon substance. These cells stain less densely than the cells of the tendon proper. More peripherally the fibrous sheath is developing.

In the extensor tendon (Fig. 10) the peripheral tendon cells remain flattened, whilst the more central cells have become rounded. Loose mesenchymal tissue separates the tendon from the perichondrium.

*Electron microscopy*

Individual cells are further separated. Intercellular matrix and fibrils have increased (Fig. 11). Cell nuclei are irregularly shaped and stain densely. Cell cytoplasm shows a well-developed endoplasmic reticulum with mitochondria, Golgi apparatus and many cytoplasmic processes. Some cytoplasmic processes surround single or small groups of collagen fibrils (Fig. 12). The fibrils, however, are still extracellular, being surrounded by invaginations of cell membrane. The diameter of the collagen fibrils now averages 39 nm with remarkably little variation. Elastic fibril bundles are still seen, sometimes at locations away from the cell membrane. Cell junctions, on longitudinal section, are seen at points of side-to-side apposition of one cell body to the terminal cytoplasmic process of an adjacent cell. At some areas within the tendon

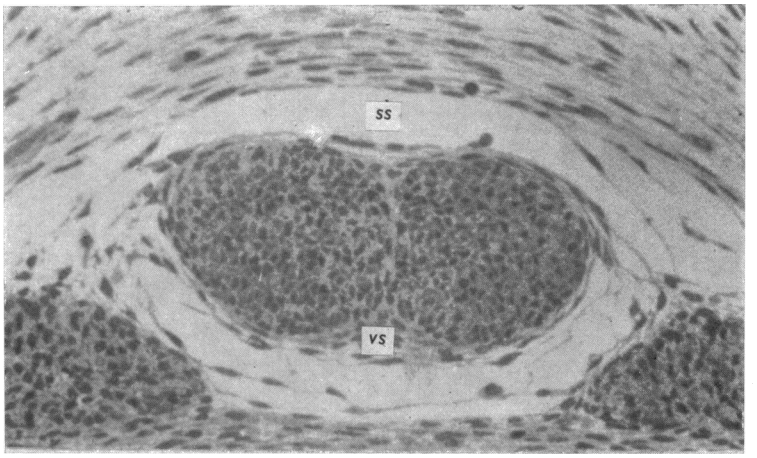


Fig. 9. Flexor tendon, 48 mm C.R.L. A synovial space (*ss*) has formed, but a fine reticulum of cells crosses the space, particularly in the mid-lateral areas. Cells continuous with the visceral synovial cells (*vs*) form a mid-line septum within the flexor tendon. The fibrous sheath is shown at the top of the illustration. × 150.

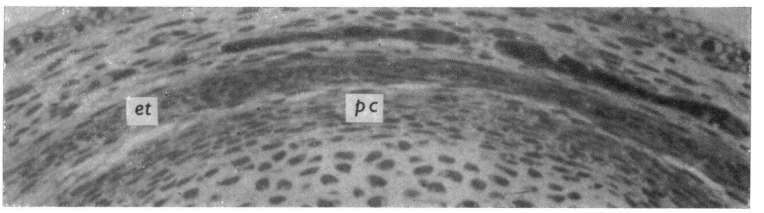


Fig. 10. Extensor tendon, 48 mm C.R.L. The tendon (*et*) is a thin strip of tissue arranged around the cartilage and its overlying perichondrium (*pc*). × 150.

substance cytoplasmic processes form bizarre patterns (Fig. 13) and here fibrils are sparse or non-existent. The visceral synovial cells have few cytoplasmic processes, whilst their cytoplasm contains only small amounts of endoplasmic reticulum and mitochondria. More peripherally, and within the synovial space, thin bands of cytoplasm cross the otherwise structureless space.

The features demonstrated reflect the organization behind the development of tendon. All cells within the tendon are at a very similar stage of development. Collagen fibrils are parallel to each other, and to the long axis of the cell, and are formed within a pre-existing space filled with some non-staining fluid or ground substance. Cell junctions (or cell contacts) remain and could provide the means whereby external forces are transmitted from cell to cell. Collagen fibrils are of constant size and at 39 nm have reached the maximum size seen in this series (i.e. up to 140 mm C.R.L.). Cells related to the synovial sheath fail to develop the complex structure shown in the tendon cells. The exact temporal relationship between the development of the synovial space and movement of the digit is not clear at the present time.

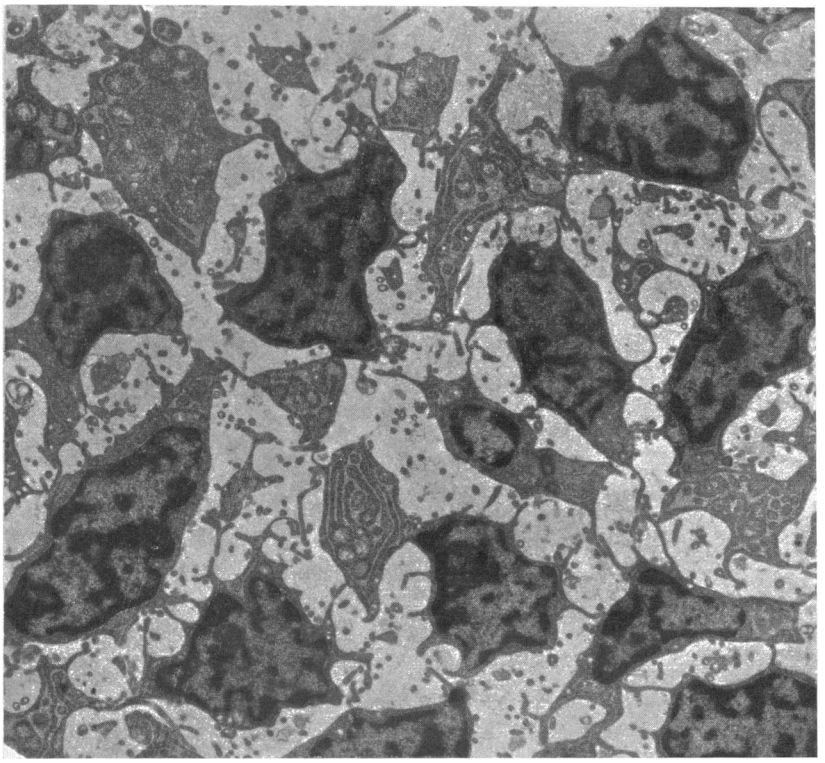

Fig. 11. Flexor tendon 48 mm C.R.L. Cells show many cytoplasmic processes and the cytoplasm contains a well developed endoplasmic reticulum. Mitochondria are visible, but not well fixed, in this specimen. × 5000.

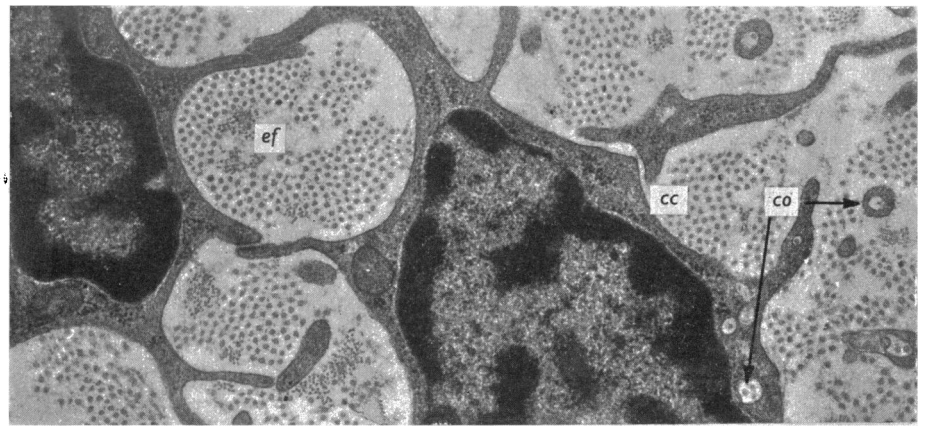


Fig. 12. Flexor tendon 48 mm C.R.L. Collagen fibrils (*co*) are present in the intercellular space and also within cytoplasmic processes and within the main cell cytoplasm. Elastic fibrils are still obvious (*ef*) and cell contacts (*cc*) are frequent. × 12500.

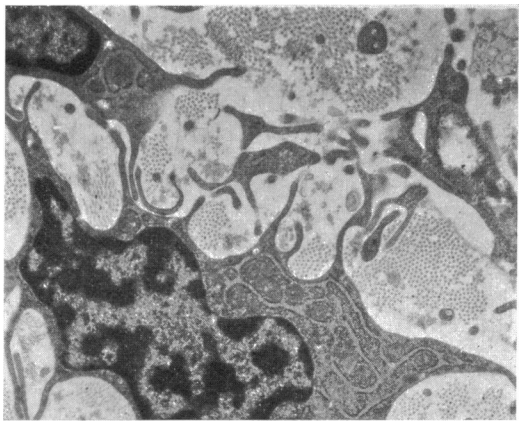

Fig. 13. Flexor tendon, 48 mm C.R.L. In situations as shown here, the cytoplasmic processes show bizarre and irregular patterns and at these points collagen fibril deposition is deficient. These areas will be seen to be related to fascicle formation within the tendon. × 7000.

### 80 *mm C.R.L.* (80 *days*)

*Light microscopy*

The flexor tendon synovial cavity is complete, the fine reticulum of cells having disappeared. The tendon is otherwise larger and shows further separation of individual cell nuclei. In the extensor tendon, local thickenings representing the central tendon and the lateral bands have appeared, and are the result of further local proliferation of cells.

*Electron microscopy*

The cell cytoplasm has a well-developed endoplasmic reticulum and Golgi apparatus, whilst the nuclei have become relatively smaller (Fig. 14). Collagen fibrils (39 nm) occupy much of the available intercellular space, but also lie in bundles seemingly surrounded by cell cytoplasm or else as single fibres within a cytoplasmic process. Elastic fibres are beginning to become amorphous (Fig. 15), i.e. they show areas where the densely staining fibrils are replaced by an unstaining amorphous material.

The cell is evidently producing collagen fibrils with precise longitudinal orientation. The shape of the cells on cross section appears, at least partially, to be determined by the disposition and density of the collagen fibrils.

### 110 *mm C.R.L.* (95 *days*)

*Light microscopy*

The visceral and parietal synovium are thicker. The tendon is dividing into smaller units or bundles (Fig. 16), a process we may call *fasciculation*. The extensor tendon also shows fasciculation. Blood vessels are seen for the first time; they lie close to the flexor tendon dorsally, but none can be identified within the tendon itself.

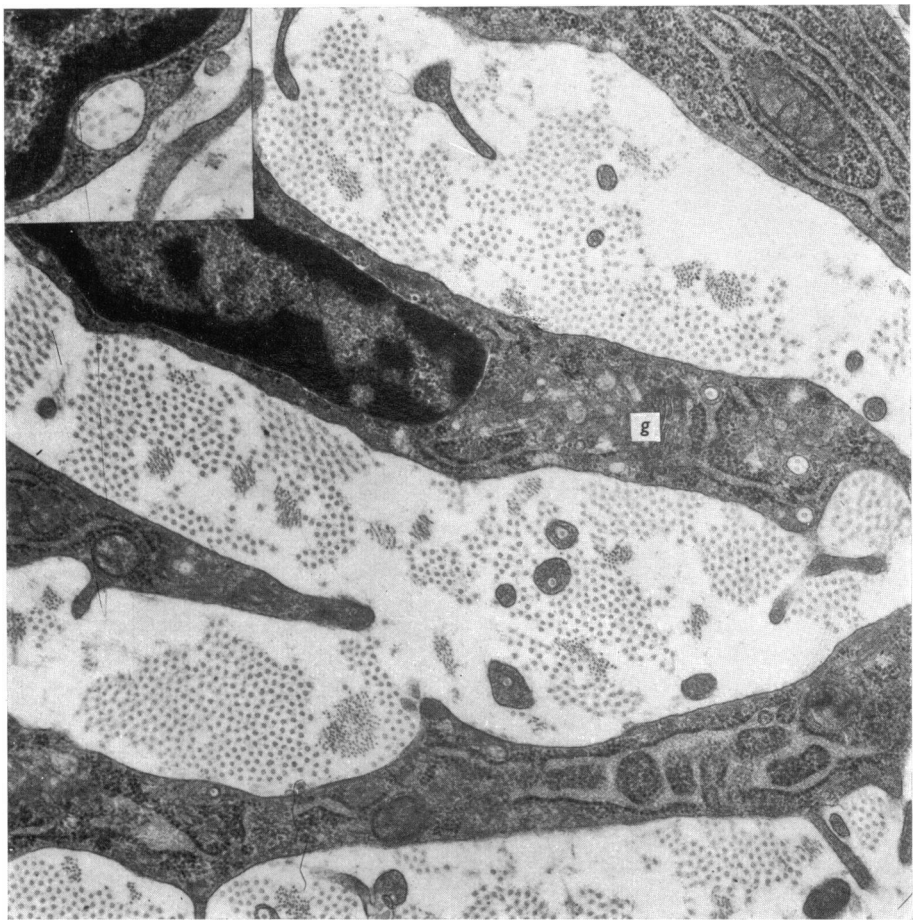


Fig. 14. Flexor tendon, 80 mm C.R.L. Cell cytoplasm is filled with endoplasmic reticulum, Golgi apparatus (*g*) and mitochondria. The inset shows that small bundles of collagen fibrils are still forming within cytoplasmic nests. × 17500.

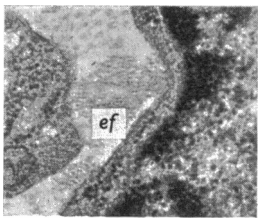


Fig. 15. Flexor tendon, 84 mm C.R.L. Elastic fibrils (*ef*) are undergoing an amorphous change as they mature. × 27500.

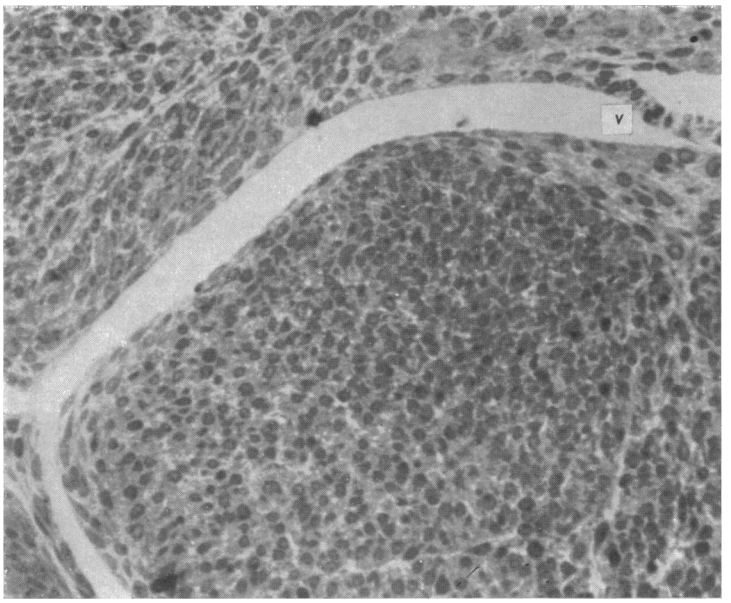


Fig. 16. Flexor tendon, 110 mm C.R.L. The tendon is splitting into smaller bundles or fascicles barely distinguishable on light microscopy. No blood vessels are seen within the tendon. The synovial space is well developed. A small vinculum (*v*) is seen dorsally. × 2500.

*Electron microscopy*

Collagen fibrils fill much of the available space between cells (Fig. 17). The fasciculation seen by light microscopy is produced by large cytoplasmic processes which encircle groups of cells and bundles of fibrils. The cells giving rise to these processes are morphologically similar to the other tendon cells. The previously noted areas showing bizarre patterns of cytoplasmic processes and an absence of collagen fibrils are related to these interfascicular areas. Elastic fibres are more amorphous than before.

The visceral synovium is now several cells thick (Fig. 18), the deepest cells producing bundles of collagen fibrils in a plane at right angles to the long axis of the tendon and these appear to bind the tendon into a compact unit.

Vascular buds are seen between the individual fibril bundles in the interfascicular space of the extensor tendon (Fig. 19). These are small and immature and in the specimen illustrated consist of a single cell with a small lumen surrounded by a basement membrane. The appearance of blood vessels within the substance of the extensor tendon indicates either that cell migration within the tendon is possible, or else that the vessels have been passively incorporated as the tendon grows.

140 *mm C.R.L.* (110 *days*)

*Light microscopy*

The flexor tendon is large, fasciculation obvious and the synovial membrane well developed (Fig. 20). Blood vessels are prominent dorsally.

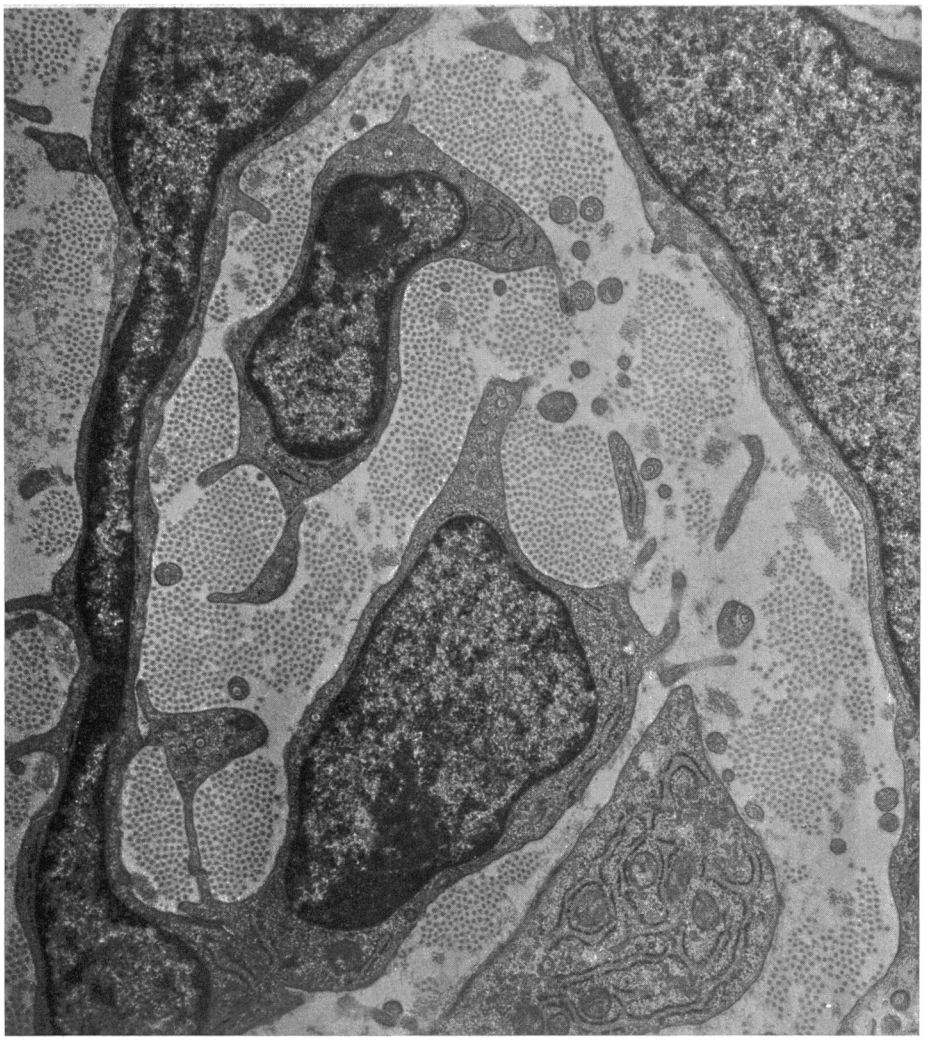

Fig. 17. Flexor tendon, 110 mm C.R.L. This small fascicle is completely surrounded by cell cytoplasm on cross section. × 13750.

*Electron microscopy*

*Flexor tendon.* Tendon cells are angular with thin cytoplasmic processes. Cell junction sites are larger and more prominent (Fig. 21). Collagen fibril size remains at about 39 nm. The cytoplasmic processes surrounding individual fasciculi are reinforced by small bundles of collagen fibrils (Fig. 22). The visceral synovium is several cells thick, but each cell does not maintain close apposition to its neighbour. No vascular buds are to be seen within the tendon.

*Extensor tendon.* The only notable feature is further development of the vascular buds (Fig. 23). Each vessel now consists of two cell layers, the new cell being the

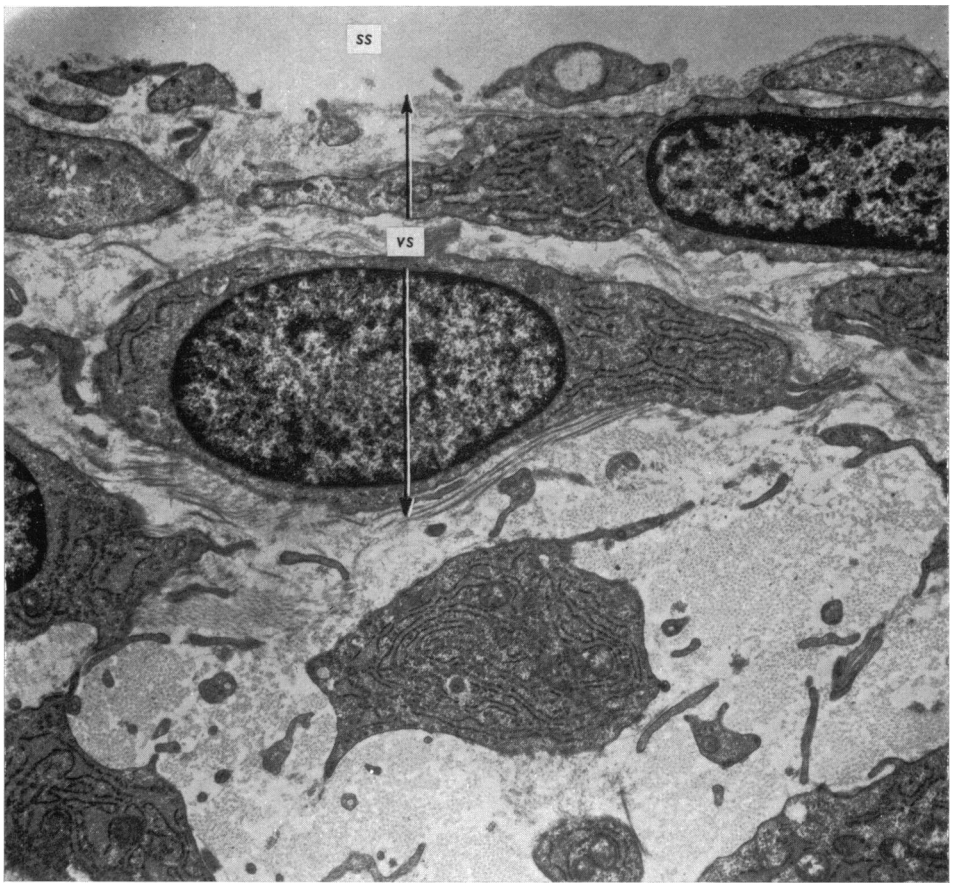


Fig. 18. Flexor tendon, 110 mm C.R.L. The synovial space (*ss*) is featureless but the visceral synovium (*vs*) consists of several cell layers and a few 'wrapping' collagen fibrils. × 7500.

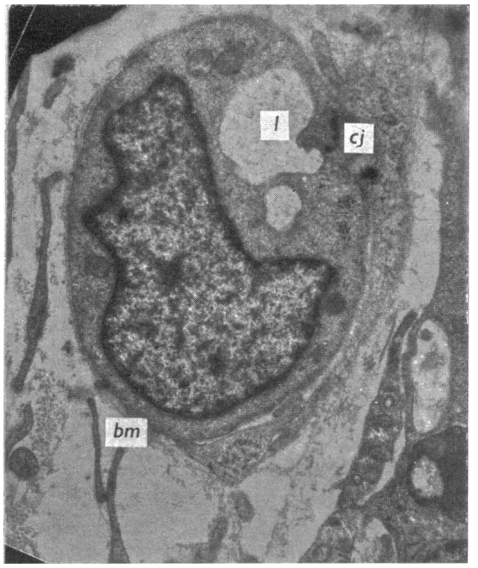


Fig. 19. Extenson tendon, 110 mm C.R.L. Blood vessel (capillary bud) within the extensor tendon in an interfascicular space. The vessel is surrounded by a basement membrane (*bm*), has a small lumen (*l*) and epithelial cell junctions (*cj*). × 8000.

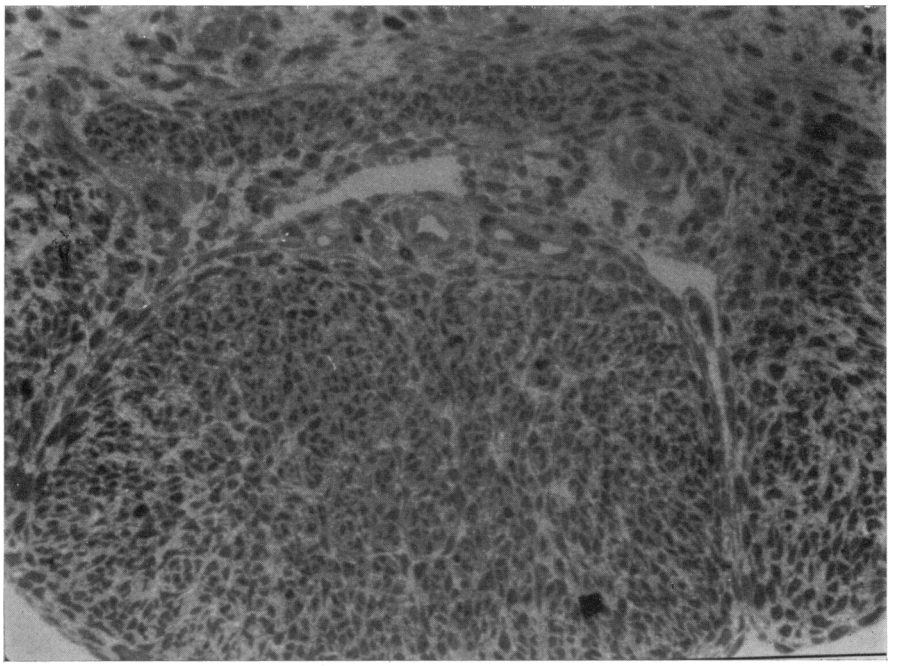

Fig. 20. Flexor tendon, 140 mm C.R.L. Prominent fasciculations are seen within the tendon and large blood vessels are seen dorsally. × 150.

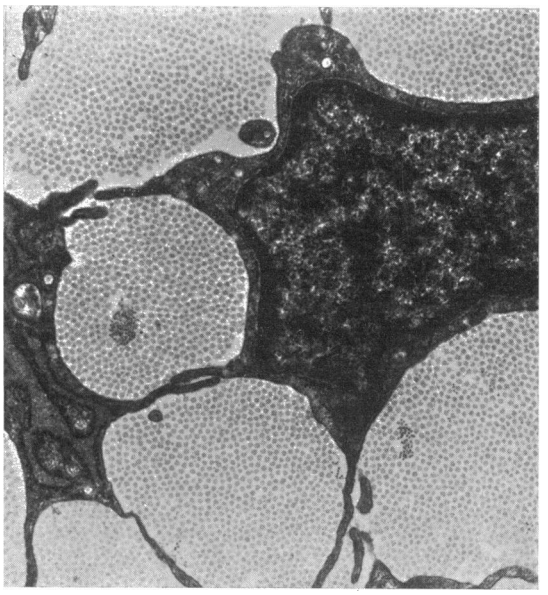

Fig. 21. Flexor tendon, 140 mm C.R.L. Collagen fibrils (390 nm) fill almost the entire intercellular space. Cells maintain contact by thin angular cytoplasmic processes. × 12000.

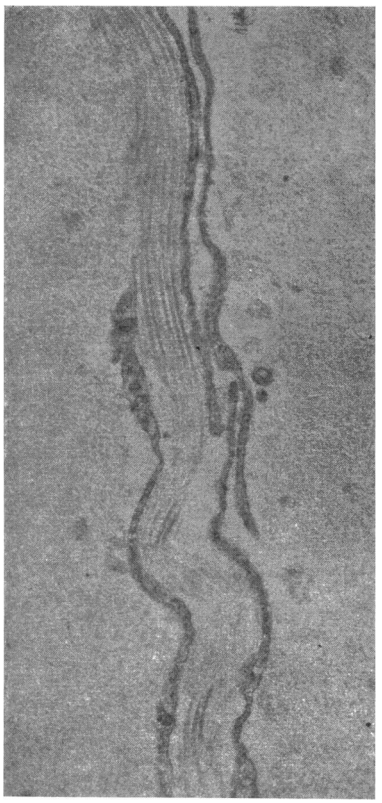

Fig. 22. Flexor tendon, 140 mm C.R.L. The attenuated interfascicular cytoplasmic processes are accompanied by bundles of collagen fibrils. × 13000.

pericyte, the original cell having an irregular lumen and specialized intercellular junctions.

## DISCUSSION

### *Development of flexor and extensor tendons compared*

Light microscopy shows the most obvious differences in development of the two tendons. Even from the earliest stages, flexor tendons on cross section are round, whilst extensor tendons are flattened around the cartilage anlage. Growth of the flexor tendon is by increasing the diameter of the tendon itself, whilst, in the extensor tendon, it is the increase in the diameter of the cartilage anlage which apparently results in, or at least induces, widening of the extensor tendon. Thickness of the extensor tendon increases as a result of hypertrophy of the mid-zone of the tendon. Electron microscopy reveals no basic differences between the morphology of the flexor and extensor tendon cells, apart from the overall shape of the cells which does vary with the overall shape of the tendon.

Mechanisms controlling cell differentiation and organ shape evidently operate from the earliest moment of tendon development. One feasible, although unproven,

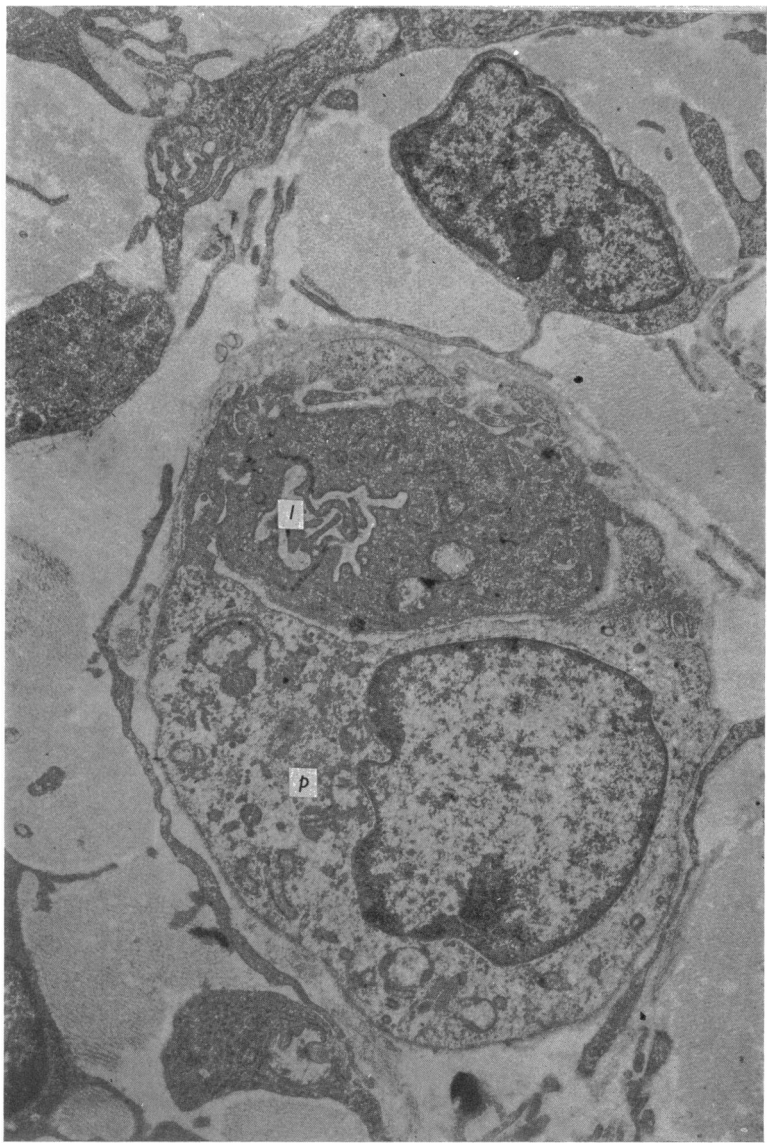


Fig. 23. Extensor tendon, 140 mm C.R.L. Vascular buds in the interfascicular space. In this section the pericyte (*p*) appears large and the endothelial cells small. The lumen (*l*) is still not large enough to support a circulation of red blood cells. × 8000.

mechanism would be the presence and location of cell junctions which could limit cell separation and thus control the overall shape of the tendon (Ross & Greenlee, 1966). Cell junctions in these specimens are shown to persist as development proceeds.

The *synovial sheath* appears early in the course of development of flexor tendons (48 mm C.R.L.). The sheath is initially crossed by a fine reticulum of cells. Spaces are seen in the mesenchyme in relation to the extensor tendons, but these are at a

distance from the tendon and possibly artefactual. The demarcation and distinction between tendon cells and cells in the surrounding mesenchyme is clear cut both on light and electron microscopy. Movement of the limb is known to commence around the time of the appearance of the sheath (Drachman & Sokoloff, 1966), but whether this is due to the formation of the sheath, which in turn allows movement, or whether movement induces these changes is at present uncertain. It is known that paralysis of the chick embryo delays the appearance of the sheath and allows the deposition of collagen fibrils within the space (Dimond, 1973).

*Collagen fibrillogenesis*

The exact mode of fibril production is at present uncertain. Fibrils may be either: (*a*) formed in the intercellular space by aggregation of macromolecules, (*b*) formed intracellularly and secreted intact, or (*c*) formed at the cell surface by a fibrillar transformation of the cell's surface (Chapman, 1962; Rhodin, 1967; Ross, 1968). The argument will probably continue until some method of visualization of the process in the living cell is developed.

In this study, single fibrils and also small bundles of fibrils look as if they lie within the cytoplasm of cell processes (Figs. 12, 14) surrounded by cell membrane. Collagen fibrils lie centrally within the process and longitudinal sections confirm that the fibril is continuous with the extracellular fibril (Figs. 25, 26). The cytoplasm appears as if it were actively peeling away from the collagen fibril, although it could be that the fibril was being engulfed by the cytoplasmic process. It is not possible to decide between the two hypotheses.

The earliest fibrils measure approximately 29 nm in diameter and are close to the cell membrane (Figs. 2, 6), but do not occupy all the available intercellular space. Fibril deposition continues, the fibril diameter and interfibrillar distance remaining remarkably constant until the available space is well filled. More space is then made available by separation of individual cells. The diameter of individual fibrils increases to 39 nm (Fig. 12) at 48 mm C.R.L. and remains at this size until at least 140 mm C.R.L. In the later stages fibrils appear to be compressing the individual cells and cytoplasmic processes (Fig. 21). This constancy in fibril size at a given stage is not seen in the developing chicken or rat tendon. At full term, collagen fibril diameter has been shown to be 500 nm (Rhodin, 1967).

*Elastic fibrillogenesis*

This is also seen within human tendons (Figs. 7, 12, 15) as in rat and chicken tendons (Beckham & Greenlee, 1975; Greenlee & Ross, 1967). The total amount is not great and the cross sectional area occupied by elastic tissue gradually diminishes with development. The significance of elastic tissue in tendons remains speculative. Elastic tissue may allow tendon to be restored quickly to a resting length by elastic recoil, perhaps aiding movement of fluid (and nutrients) within the tendon.

*Tendon vascularity*

Light microscopy fails to show blood vessels within the substance of either flexor or extensor tendons in this series, although vessels are clearly visible in the surrounding tissues and vincula (Fig. 20).

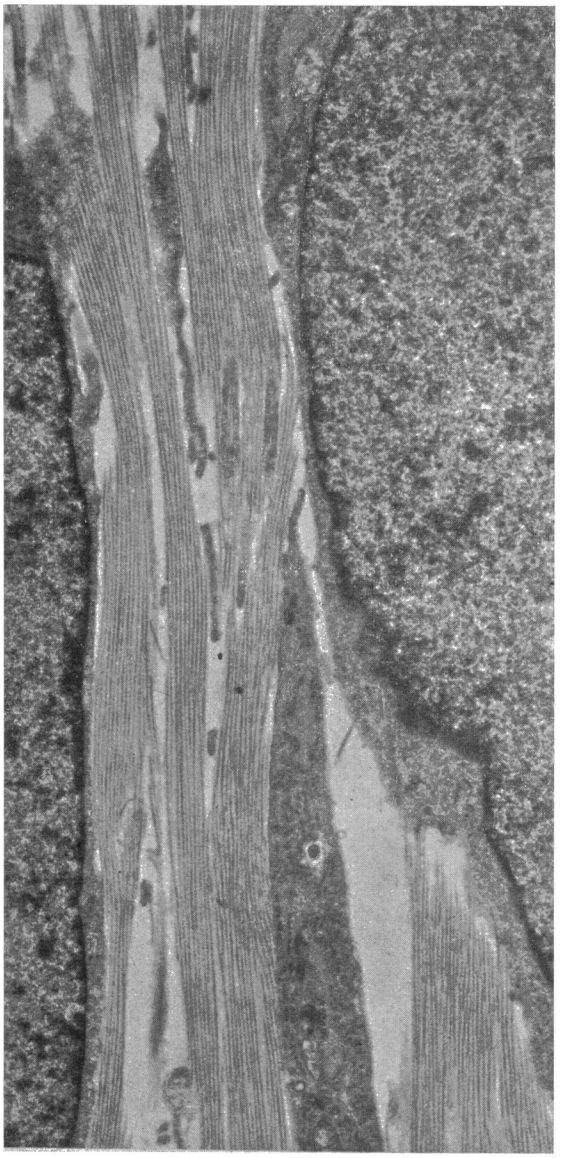

Fig. 24. Flexor tendon, 140 mm C.R.L. Longitudinal section confirms that collagen fibrils are parallel, except where they are separated by cytoplasmic processes. × 7000.

Electron microscopy, on the other hand, shows that vascular buds appear between bundles of fibrils in the extensor tendon from 110 mm C.R.L. onwards. These vascular buds are immature, and the lumen is not large enough to support a circulation of red blood cells, but their appearance confirms the potential for a capillary circulation within this tendon. Their appearance also demonstrates that cellular movement may occur along the tendon between the fasciculi. Vessels will appear later within the

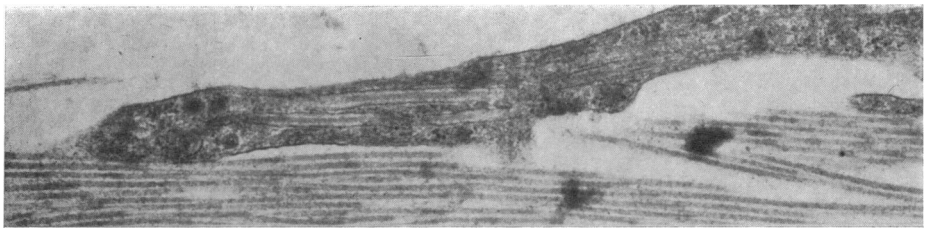

Fig. 25. Flexor tendon, 140 mm C.R.L. Longitudinal section of a cytoplasmic process showing the 'enclosed' collagen fibrils. ×20000.

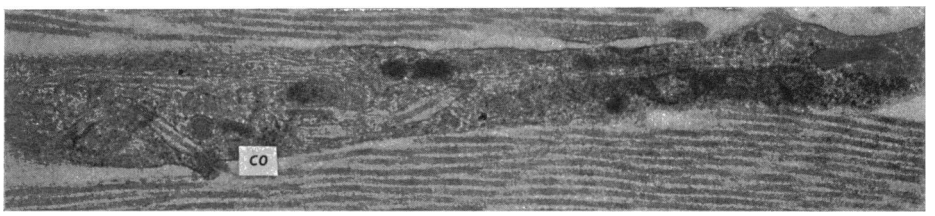


Fig. 26. Flexor tendon, 140 mm C.R.L. Fortuitous longitudinal section showing a single collagen (*co*) fibril passing out of the cytoplasmic process. ×20 000.

flexor tendon, but the difference in the degree of vascularity between flexor and extensor tendons seems to be maintained to maturity, when it can be demonstrated by microvascular techniques (Brockis, 1953; Chaplin, 1973; Smith, 1965). One reason for this difference in vascularity could be that the two tendon types have different nutritional requirements. However, the appearance of both tendons under the electron microscope is very similar, even to cytoplasmic details and the size of individual fasciculi. In contradistinction, the ground substance, though it must exist, is not visualized under the electron microscope; differences between their respective ground substances could conceivably produce differences in the diffusion rates of nutrients throughout the tendon and, hence, different vascular requirements.

*Cell organization*

The morphological appearances of the early cells are characteristic of cells producing protein for cell growth and division. The transition from this state to cells equipped to produce extracellular protein occurs smoothly and all cells are at a similar stage of development at one particular time. Precise control is also exerted over the orientation and size of individual fibrils at all stages of development. Fibrils remain parallel (Fig. 24), of equal size and with an even interfibrillar distance, except when separated by cytoplasmic processes.

The later appearance of fasciculation is interesting and is similar to the fasciculation seen in the chick (Greenlee *et al.* 1974). Each bundle of fibrils and cells is initially wrapped by cytoplasmic processes, which are later reinforced by collagen fibrils. Several advantages of fasciculation are envisaged. The strength of the tendons, as a whole, is increased whilst its flexibility is enhanced. Furthermore, fasciculation may

be important for nutrition, the interfascicular space being useful for diffusion of nutrients and the ingrowth of blood vessels.

*Cell mobility*

All living cells are theoretically mobile. Tendon cells show cytoplasmic structures known to be associated with movement, i.e. flagelli, centrosomes and intracytoplasmic fibrils. It has not been determined whether tendon cells can move within the tendon along the collagen bundles, or whether movement is limited to the cytoplasmic processes of the cell, the body of the cell being 'trapped' by extracellular deposition of fibrils. Space is available for cell migration within the tendon, initially, because the extracellular space is not completely filled with collagen fibrils. Later, when this space is more densely packed with regularly orientated fibrils, fasciculation may at least allow some movement of the cells.

*Development of human flexor tendons compared with that in chicken and rat*

Tendon cell morphology in both the rat and the chicken is strikingly similar to that of human tendons (Greenlee & Ross, 1967; Greenlee *et al.* 1974). The chick flexor tendon forms internal fascicles at about the 13th day (the chick has a 21 day gestation period) which carry a complex blood supply to their tendons. No blood vessels were seen in the rat tendon at birth, or in 30 day old animals.

In the rat, collagen fibril size was constant at 40 nm at birth but increased in size to between 80 and 160 nm at 30 days. At this time fibril size was less homogenous. In the chick embryo, fibril size is uneven throughout development. Also, fibrocartilage develops along the surface of the tendon which overlies a pulley, and probably represents a specific tissue adaptation to prevent excessive wear.

## SUMMARY

The development of human digital flexor and extensor tendons from 40 days to 112 days of gestation is described.

The differentiation of the cell, the formation of collagen fibrils, and their organization into a relatively complex tendon organ are described.

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