A mechanism of formation of desmosome-like structures between synovial intimal cells

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Summary. Desmosomes or desmosome-like structures do not occur between normal human synovial cells but such structures do develop between the synovial cells in cases of traumatic arthritis, rheumatoid arthritis and villonodular synovitis. Morphological evidence is presented suggesting that such structures develop as a result of the interaction of fibrin trapped between synovial cells and the plasmamembrane of these cells.

Synovial cells are set apart in a matrix so, as a rule, no cell junctions are seen. In some species and in certain situations where the synovial cells become closely packed, cell junctions may develop. Desmosome or desmosome-like junctions are relatively frequent in the synovial membrane of the rat[1] and cat[2] and they may also occasionally be found in the rabbit and the calf[2,3].

No cell junctions have been found in the normal human synovial membrane but they are often seen in pathological states where a hyperplasia of the synovial intimal cell has occurred; e.g. in traumatic arthritis, rheumatoid arthritis and villonodular synovitis[4–7].

The manner in which such junctions develop is not known and no mechanism to explain this phenomenon has been proposed. We have now examined this problem in pathological human synovial membranes and concluded that at least in some of these cases desmosome-like structures are in fact a reaction of the synovial cell membrane to fibrin trapped between the synovial intimal cells.

The main reason for this belief stems from the fact that we have noted appearances which can be interpreted as successive stages in the development of desmosome-like structures from fibrin deposits which at times show the characteristic 24-nm banding (figure 1). We have also found that

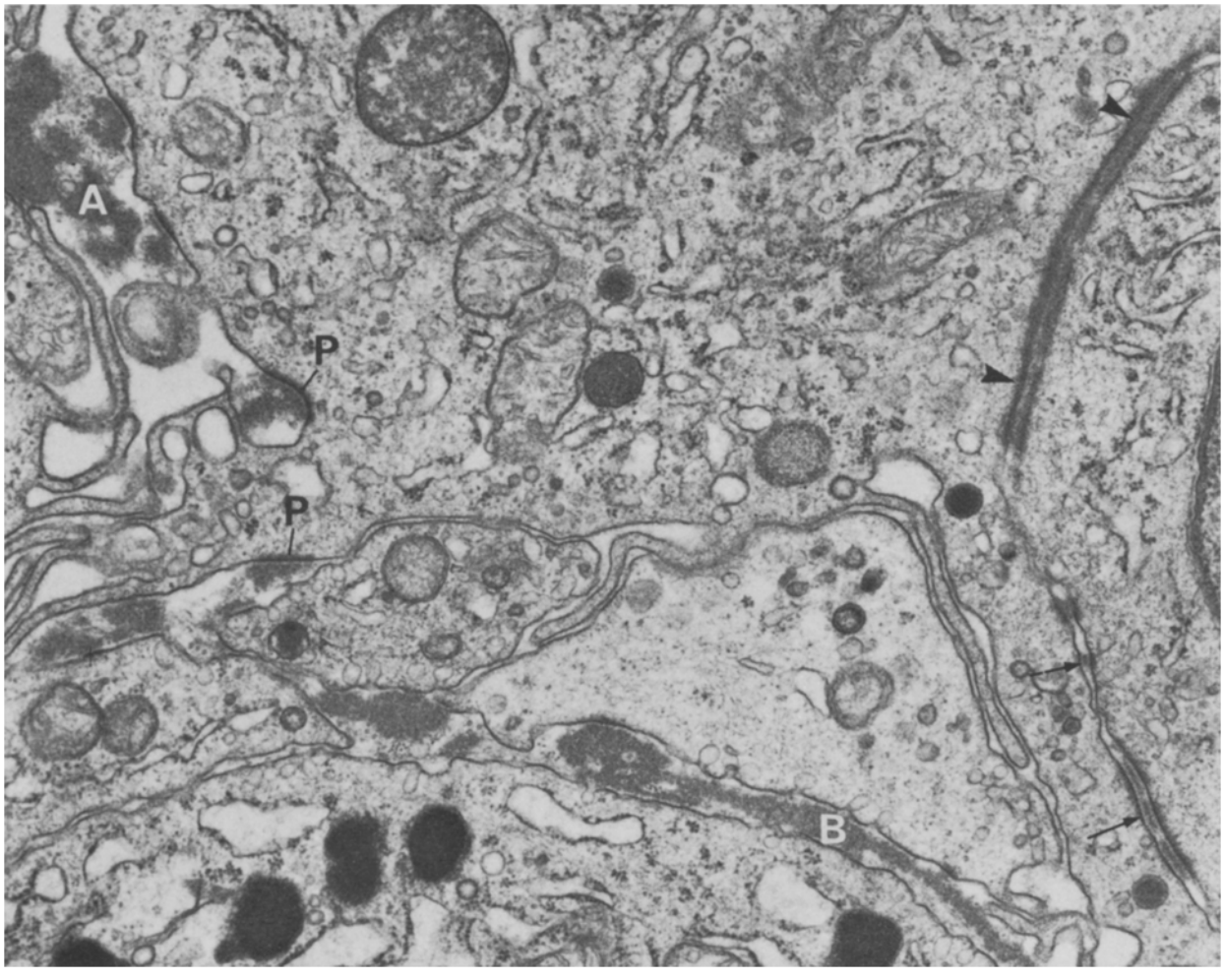

Fig. 1. Synovial membrane from a case of villonodular synovitis. A mass of fibrin (A) is seen amongst the synovial cells situated near the joint space which lay to the left of the picture. In some places dense plaques (P) have formed where the fibrin abuts against the synovial membrane. A band of similar material (B) is seen between more deeply placed synovial cells and at an even deeper level desmosome-like (arrows) structures have formed where the intercellular space contains material acceptable as attentuated fibrin. Also seen is a rather long junction-like formation where the plane of section is such that the contents of the intercellular space are not clearly revealed. × 24,000.

when fibrin lying on the surface of the synovial intima is apposed to the cell a dense filamentous coat may develop on the cytoplasmic aspect of the plasma membrane (figure 2). Such a phenomenon is at times a prelude to the formation of partially coated vacuoles by which synovial cells endocytose fibrin from the joint space[8].

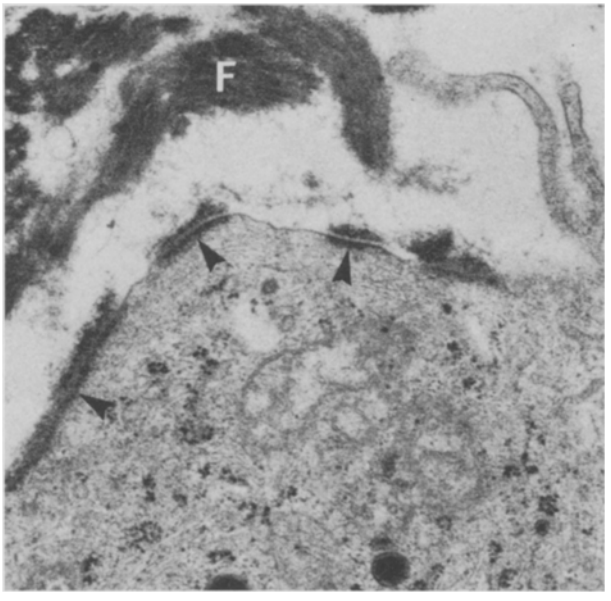

Fig. 2. Synovial membrane from a case of rheumatoid arthritis showing fibrin (F) deposits in the joint space, and focal plaques (arrowheads) that have developed on the surface of a synovial cell. The material forming the external coat of the plaque is similar in appearance to the fibrin in the joint space. Note also the dense coat on the cytoplasmic surface of the plasmamembrane and the lucid interval between the 2 dense structures comprising the plaque. ×29,000.

Yet another fact that supports our hypothesis is that haemorrhage and/or fibrin deposition occur in the pathological states (mentioned above) where desmosomes or desmosome-like structures have been found between human synovial intimal cells. It seems to us that if fibrin is trapped between 2 synovial cells and a filamentous coat develops (as in figure 2) on the cytoplasmic sides of the adjacent plasma membranes then an appearance minicking a desmosome will be created (as in figure 1).

It would appear that besides the synovial membrane there may be other tissues where also desmosome-like structures may develop in the manner described here. For example structures resembling intermediate junctions and desmosomes (remarkably similar to those seen in figure 1) have been reported in 3-methylcholanthrene-induced mouse sarcoma[9] and one may speculate that haemorrhage may have occurred in the tumour and led to the production of such structures.

Our thesis regarding the formation of desmosome-like structures in certain pathological synovial membranes of man leaves unexplained why desmosomes or desmosome-like structures occur in the normal synovial membrane of some animal species and not others. It seems to us that more than one mechanism may be involved and that if a close association of synovial cells occurs this may trigger some hitherto unknown mechanism(s) of junction formation.

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Effects of exogenous thyroxine on the surface morphology of the developing chick anterior corneal epithelium[1]

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Summary. The production of microvilli on the developing chick anterior corneal epithelium is drastically accelerated by the administration of exogenous thyroxine and the effects are seen as early as 2 days after injection. Thiouracil administration slightly retards the production of microvilli though its effects are not so pronounced.

The cornea of the chick undergoes a dehydration and becomes transparent between the 14th and 19th day of incubation and it has been shown that these phenomena are under the influence of thyroxine[2,3]. It has also been shown that the administration of exogenous thyroxine to the chick at 10 or 12 days of incubation results in a decreased corneal thickness and a precocious development of intercellular complexes responsible for the barrier function of the epithelium and endothelium[4,5]. More recently scanning electron microscopy has shown that up to about the 15th day of incubation the anterior corneal epithelium is characterized by an ever increasing number of microvilli[6,7]. It was of interest, therefore, to see if this developmental parameter was influenced by exogenous thyroxine.

Fertile chicken eggs were incubated at 37.5 °C and 82% relative humidity in a circulating air incubator. Thyroxine (DL-thyroxine; Sigma) was dissolved in 0.1 N NaOH (prepared with 0.9% saline) and the pH was adjusted to 7.8–8.2 with 1 N HCl. Thiouracil (2-thiouracil; Sigma) was prepared as a suspension in 0.9% saline. After 9 days of incubation, a window was made through the shell and shell membranes and 1 µg thyroxine, 10 mg thiouracil, or an equal volume (0.5 ml) of the drug vehicle was injected directly onto the chorioallantois. Unoperated animals served as normal controls. The animals were sacrificed at 2, 4, or 6 days after drug treatment and the corneas were processed for scanning electron microscopy. The tissues were fixed according to the method of Hirsch and Fedor-