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Myoendothelial contacts in the small arterioles of human kidney

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Summary. Human renal biopsies were examined electron microscopically to investigate the intercellular relationships between endothelium and smooth muscle in renal arterioles. Three types of contacts were seen occurring through perforations in the basal lamina. These were classified by their origin either, from an endothelial cell, from a smooth muscle cell or from both. The cell processes involved were usually irregular but some were identified as club-shaped. The nature of the contacts was predominantly via simple appositions with an intercellular space of 6.9–13 nm. These myoendothelial contacts may play an important role as sensors of hypertensive load.

Key words: Human renal vessels – Myoendothelial contacts – Hypertension

Introduction

Myoendothelial contacts have been thought to be the mediators of blood-borne humoral signals involved in the control of cerebral (Dahl 1973) or peripheral (Rhodin 1967) vascular tone. They are now also considered to be involved in the myogenic response of vascular smooth muscle (Johnson 1980; Edwards 1983) and the contractile responsiveness of smooth muscle cells in large and small arteries may be co-ordinated in part via the endothelium. Although the mechanisms involved in the auto-regulation of kidney blood flow have been much discussed (Edwards 1983; Gilmore et al. 1980), few investigations on myoendothelial contact in the small vessels in the human kidney have been reported (Biava and West 1966; Jacobsen et al. 1966) and only a brief description of such contacts was given.

In this study, the relationships between endothelial and smooth muscle cells in human renal vessels will be described.

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Materials and methods

From a series of 60 renal biopsies, 7 were selected for this study as sufficient tissue remained for detailed examination (Table 1). Biopsies were examined by light microscopy and immunohistochemistry using the peroxidase-antiperoxidase technique.

A small portion of the material was removed for electron microscopy. Fixation was with 4% paraformaldehyde phosphate buffer (pH 7.4) for 1.5 h, the biopsies were post-fixed for 1.5 h in 1% osmium tetroxide, then dehydrated with graded series of ethanol and embedded in araldite. Thin sections were cut with a Reichert OMU4 ultramicrotome, mounted on copper grids and stained with uranyl acetate and lead citrate, before examination in a Hitachi H500 transmission electron microscope.

Of the 7 patients whose biopsies were examined, 2 were normal, 1 chronic hypertensive changes, another IgA nephropathy, another recurrent crescentic glomerulonephritis and 2 showed focal changes.

Table 1. Details of cases studied

Renal biopsy	Sex	Age	Diagnosis (based on immunohistochemistry, EM and light microscopy)
1	M	58	Recurrent crescentic glomerulonephritis
2	M	26	Normal
3	M	14	IgA nephropathy
4	F	37	Normal
5	M	57	Focal segmental necrotising glomerulonephritis
6	F	68	Focal glomerulosclerosis
7	M	52	Hypertension

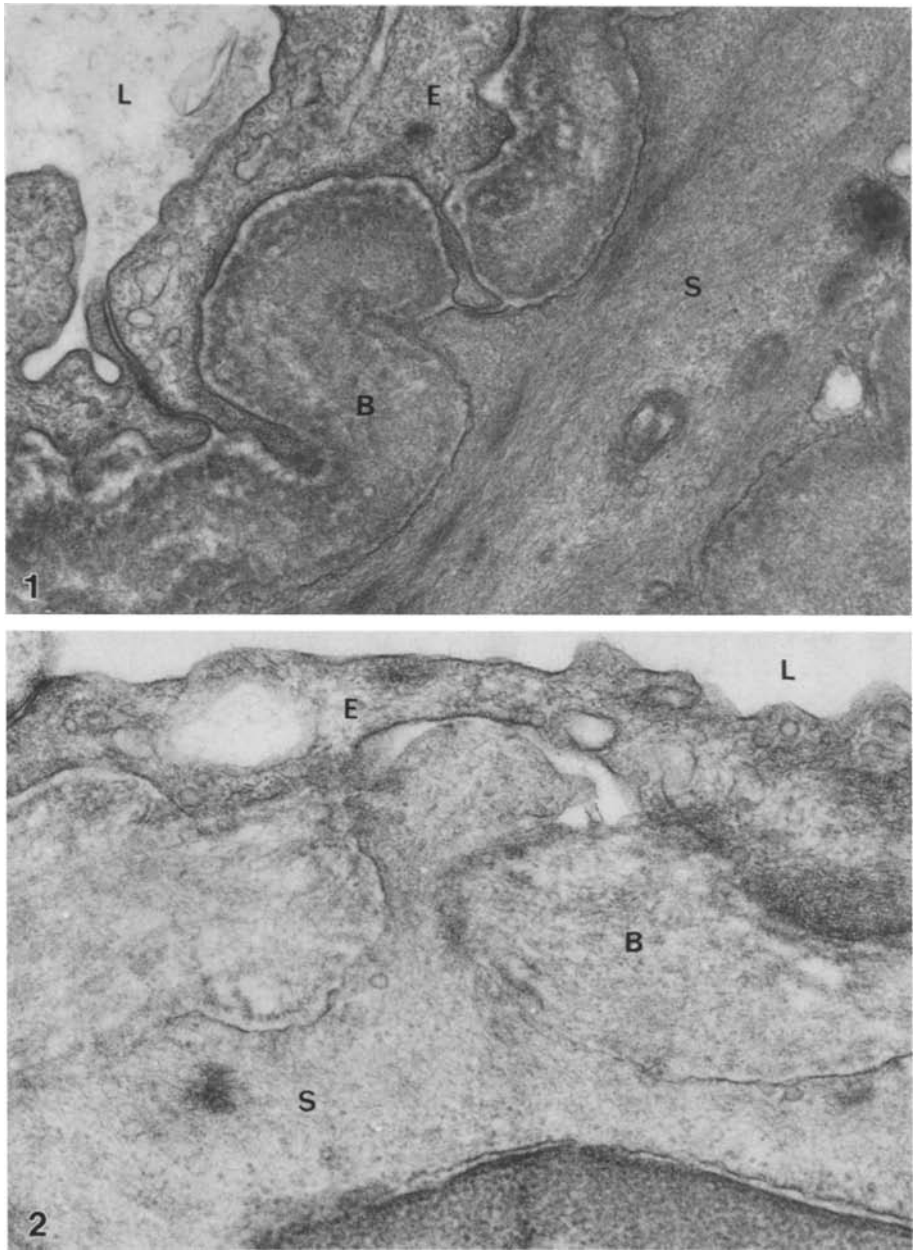

Fig. 1. An arteriole from hypertensive kidney in which a process from an endothelial cell (E) extends through the basal lamina (B) to make a contact with a smooth muscle cell (S). Biopsy No 7. ×63000

Fig. 2. Myoendothelial contact showing a club-shaped cytoplasmic process from a smooth muscle cell (S). B=Basal lamina; E=Endothelial cell; L=Lumen. IgA nephropathy, biopsy No 3. ×54000

Results

Arteriolar structure is well illustrated in the material. Peripheral to a single layer of endothelial cells is a well defined basal lamina and one or more layers of smooth muscle cells. The smooth muscle cells are separated from one another by collagen, elastic fibres and other constituents of the extracellular matrix. Contacts between smooth muscle cells and endothelial cells are irregularly distributed along the vessel wall. Three principal types of myoendothelial contacts, passing through the basal lamina, are observed:

a) Cytoplasmic projections originating from the endothelial cells (the majority) (Fig. 1).
b) Cytoplasmic projections originating from the smooth muscle cells (less common) (Fig. 2).

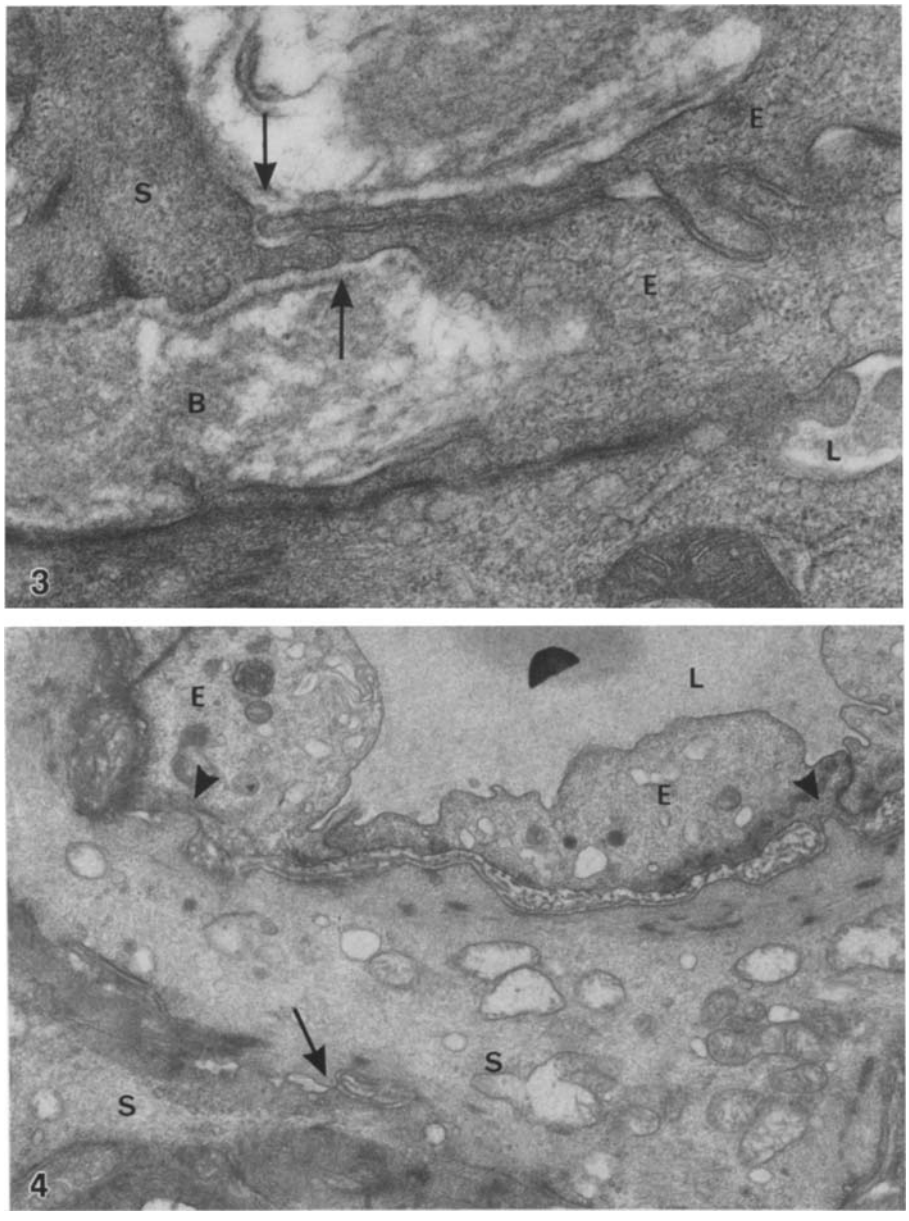

Fig. 3. Close contacts (*arrows*) between two endothelial cells (E) and a smooth muscle cell (S), consisting of narrow cytoplasmic projections. B = Basal lamina; L = Lumen. Focal segmental necrotizing glomerulonephritis, biopsy No. 5. × 54000

Fig. 4. Two musculoendothelial contacts (*arrow heads*) and cell to cell contacts between smooth muscle cells (*arrow*). E = Endothelium; B = Basal lamina; S = Smooth muscle; L = Lumen. Focal glomerulosclerosis, biopsy No 6. × 18600

c) Processes originating from both cells (rare) (Fig. 3).

The cytoplasmic processes of the two cell types were generally irregular in size and shape although some of them appeared to have a club-shaped configuration.

Occasionally myoendothelial contact was formed by delicate finger-like processes (Fig. 3) from both cells. Some cell/cell contacts involve more than one pair of cells (Fig. 4).

In both normal kidneys and those with glomerulonephritis, the contacts between endothelial and smooth muscle cells are simple appositions. The intercellular space is 6.9–13 nm and there is no membrane or cytoplasmic specialization (Fig. 5). The hypertensive vessels show myoendothelial contacts with some electron dense material on the cytoplasmic side of smooth muscle cells with signs of activation (Fig. 6). These cells show an increase of the cytoplasmic organelles and partial disap-

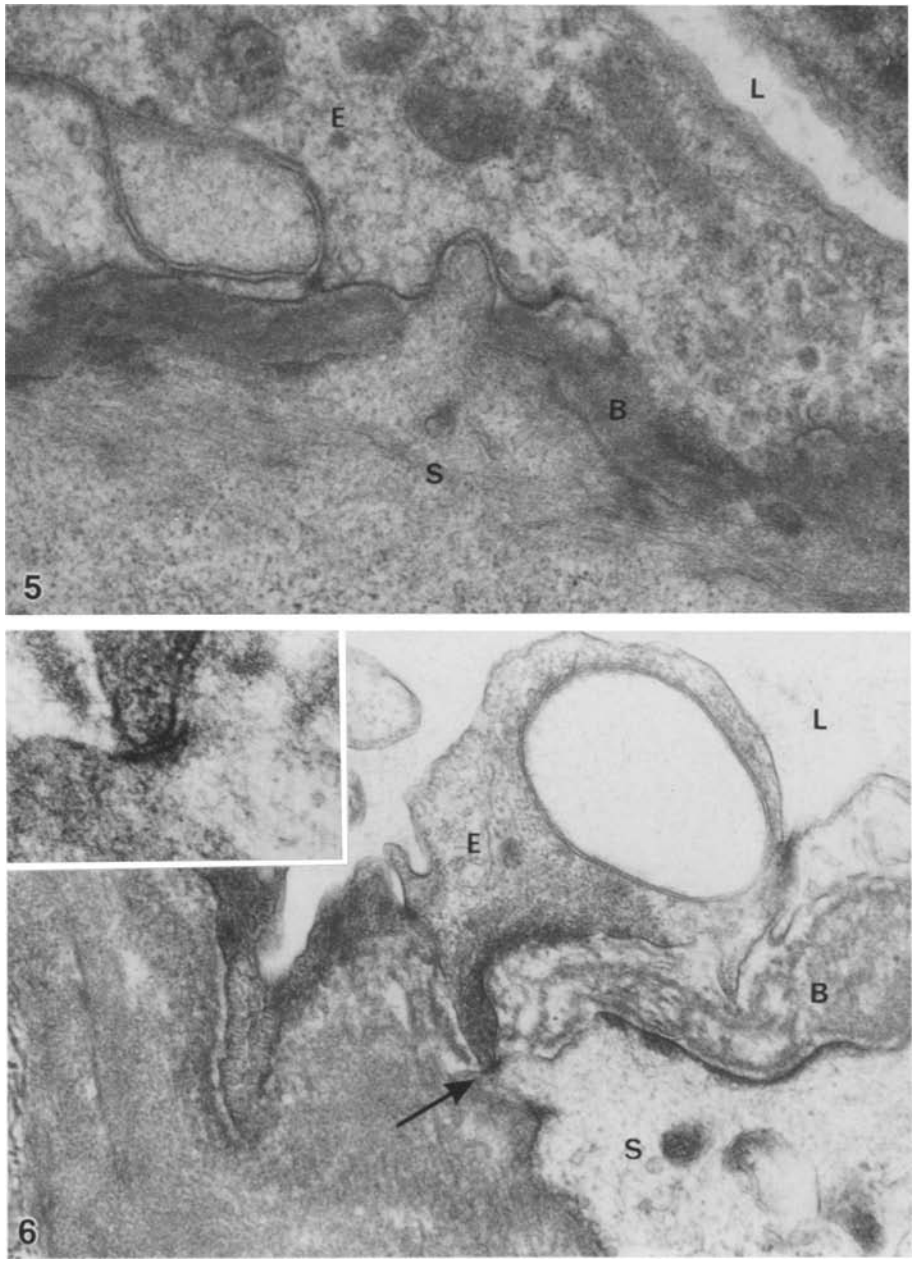

Fig. 5. Simple apposition in myoendothelial contact of normal human kidney. E = Endothelium; B = Basal lamina; S = Smooth muscle; L = Lumen. Biopsy No 4. × 42000

Fig. 6. Myoendothelial contact in hypertensive arteriole (*arrow*). L = Lumen; E = Endothelium; S = Smooth muscle; B = Basal lamina. Biopsy No 7. × 27000. Insert × 90000

pearance of myofilaments, accompanied by increased extracellular matrix production.

Discussion

The present results have demonstrated that there are close contacts between endothelial and smooth muscle cells in the small arterioles of human kidney. Three patterns of contacts were seen depending on the apparent origins of the cytoplasmic projections and simple appositions were identified as the predominant form of myoendothelial contact. Although the myoendothelial contacts of diseased and normal kidneys show no mayor structural differences, the simple appositions in some hypertensive vessels show electron dense material in the

form of a loosly woven submembranous mat in smooth muscle cells, with partial disappearance of myofilaments. Simple appositions with increased cytoplasmic electron density have some resemblance to intermediate junctions, where there is association with actin microfilaments (Geiger et al. 1983).

In earlier studies on the vessels of the fascia of the rabbit medial thigh muscles, the simple appositions observed, in myoendothelial contacts have been considered to be the same as nexus or tight junctions (Rhodin 1967); our observations show that the contacts do not form any of the well known junction types (Gabella 1981). In rat, mouse and rabbit some workers have found nexus junctions at site of myoendothelial contacts (Spagnoli et al. 1982; Taugner et al. 1984), however, in the human kidney the few reports available provide no morphological details (Biava and West 1966; Jacobsen et al. 1966).

Club-shaped myoendothelial contacts are also discussed in the context of the myogenic response of the vascular smooth muscle cells in the Bayliss mechanism (Bayliss 1902), as the method of autoregulation of vascular beds. Berry (1978) has shown the role of vessel wall tension in establishing medial structure and Bouskela and Wiederhielm (1979) have suggested that the contacts are the morphological basis of the "tension sensor" in the vessel wall. Alterations of the mechanical properties of the media may certainly affect the vessel's response to load in a way which seems to be locally determined (Berry et al. 1981).

In more recent work, co-cultures of endothelial and vascular smooth muscle cells have been used to investigate vascular smooth muscle cell differentiation (Chamley-Champbell and Campbell 1981), growth control (Van Buul-Wortelboer et al. 1986; Russell 1986) and lipoprotein metabolism (Davies et al. 1985). The interdependence demonstrated in these experiments is also required for many physiological responses of vessels; Furchgott and Zawadazki (1980) have shown that the relaxation response of rabbit aorta to acetylcholine depends on the presence of endothelial cells.

If these contacts represent a tension sensor which communicates with endothelial cells, experiments resulting in changes in vessel wall stress may alter their form.

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