Differences in the Numbers of Fenestrae Between the Arterial and Venous Ends of Capillaries in the Adrenal Cortex

The capillaries in many tissues have numerous fenestrae penetrating the peripheral cytoplasm of their endothelial cells. It has been suggested that these fenestrae allow large molecules to pass from the tissue to the blood[1,2]. (This is in addition to passage via the lymphatics.)

For this hypothesis to be correct there are a number of theoretical prerequisites that must be satisfied. Firstly, fenestrae must be permeable to proteins. Despite some early contrary reports[3-5] this is now established[6,7]. Secondly, according to Starling's hypothesis, the net hydrostatic-osmotic pressure at the arterial limbs of capillaries is directed outwards and at the venous limbs it is directed inwards. Thus the overall flow of extravascular fluid through any tissue will be from the arterial to the venous limbs of capillaries. This bulk-flow will carry proteins[8], which have low diffusion velocities, towards the venous limbs. Here, they will become concentrated because the fluid can re-enter the vessels through the closed endothelial junctions[7,9-11], which are too narrow for the proteins. It would be necessary, therefore, for fenestrae to be concentrated on the venous limbs of the capillaries. This is the case in capillaries of the rete mirabile of the renal medulla[12] and swim bladder[13], in the intestinal villus[2], in the ciliary plexus[15], and in subcutaneous capillaries[14]. The main objective of this investigation was to see if a similar arrangement existed in the capillaries of the major kind of tissue so far unstudied – viz. the endocrine system, and in particular the adrenal cortex.

Adrenal glands were taken from 10 adult white mice (~20 g) and fixed in glutaraldehyde and osmium tetroxide. The specimens were then dehydrated and embedded in araldite by the usual methods. During dehydration they were stained with uranyl acetate, and the sections were stained with lead citrate. Magnifications were checked with a grating replica. The vascular pattern in the adrenal cortex of the mouse made it possible to identify the different ends of the capillaries: the capsule contains numerous arterioles and an extensive network of capillaries, which branch into a denser mesh of vessels imme-

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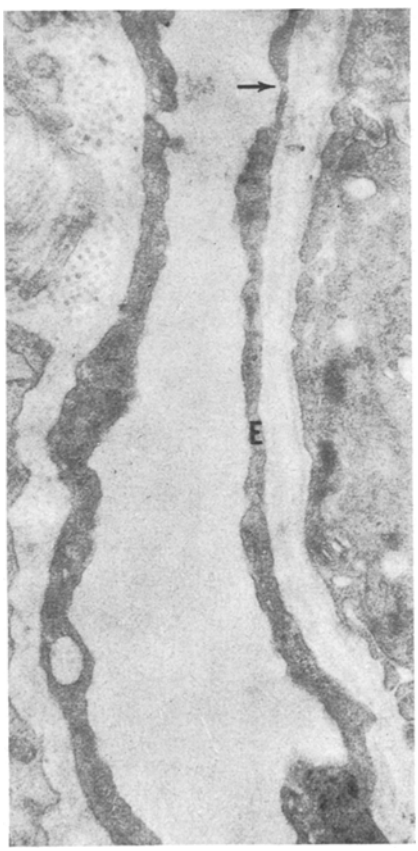

Fig. 1. Arterial limb of a capillary. The endothelium (E) is relatively thick and there is only one fenestra visible (arrow). × 25,000.

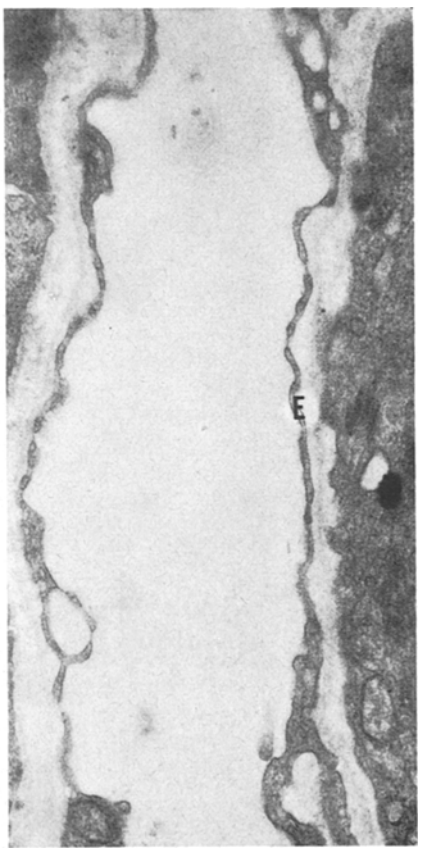

Fig. 2. Venous limb, showing the plentiful thin endothelium and the frequent fenestrae. × 25,000.

Results of measurements

		Arterial end of capillaries	Venous end of capillaries	Significance of difference *F*-test	*t*-test
Endothelium	Ratio of thin endothelium to total endothelium	0.219 (0.0476)	0.623 (0.0306)	NS	[c]
	μ^2 of endothelium per μ^3 of tissue	2.36 (0.117)	2.33 (0.122)	NS	NS
Fenestrae	Diameter	61.9 (1.58) μ	73.0 (2.21) μ	[a]	[c]
	Proportion of fenestrae having diaphragms	0.938 (0.0077)	0.930 (0.0081)	NS	NS
	No. of fenestrae per μ of endothelium	0.883 (0.237)	3.803 (0.839)	[c]	[c]
	No. of fenestrae per μ (omitting perikaryon)	0.909 (0.242)	3.90 (0.836)	[c]	[b]
	No. of fenestrae per μ of thin endothelium	2.72 (0.487)	4.76 (0.221)	NS	[b]
	No. of fenestrae per μ^3 of tissue	41.7 (11.1)	177.2 (40.4)	[c]	[c]
Junctions	No. of junctions per μ (omitting perikaryon)	0.0976 (0.0129)	0.0477 (0.0087)	NS	[b]

Figures in brackets are the Standard Errors. NS, $p > 0.05$. [a] $0.05 > p > 0.01$. [b] $0.01 > p > 0.001$. [c] $0.001 > p$.

diately below the capsule[15]. From this sub-capsular network, arise straight capillaries which cross the cortex and converge into venules in the deep cortex. Thus the sections of capillaries immediately below the capsule are of the arterial limbs while those deep in the cortex are of the venous limbs. Sections of 5 arterial and 5 venous limb capillaries from each gland were chosen at random, photographed at $\times$ 5,850 and enlarged $\times$ 3. Any with technical faults were rejected. From the remainder 2 were selected at random from each end of the 10 glands. Fenestrae were counted and the lengths of thick and thin endothelium measured. (Thin endothelium was taken as being < 100 μ thick – i.e. it was capable of having fenestrae.) In addition, 100 arterial and 100 venous fenestrae were photographed at $\times$ 28,600 and enlarged $\times$ 3. Their diameters were measured and the presence or absence of diaphragms noted. To estimate the number of fenestrae per μ^3 of tissue, we photographed random fields (856 μ^2) in the region of arterial and venous limb capillaries and used the section thickness ($\sim$50 μ) to determine the volume of tissue.

The results are shown in the Table. Fenestrae were about $\times$ 4.3 more common in venous limb capillaries than they were in the arterial limbs. Thin endothelium was also more frequent in the venous limbs than in the arterial ones. More than 90% of the fenestrae at both arterial and venous ends possess diaphragms. (It is believed that these produce molecular sieving which allows the bulk-flow of fluid to carry proteins into venous fenestrae and which inhibits the outward diffusion of plasma proteins[2].)

The higher concentration of fenestrae of the venous limbs is consistent with the hypothesis that one of their functions is to remove excessive large molecules from the tissues. It corresponds to what has been found in the other main regions where fenestrae occur[2,12–15].

The fenestrae on the arterial limbs cannot be involved in the clearance of large molecules. In fact, they are absent from capillaries of the renal medulla[12], swim bladder[13] and skin[14], and are much less frequent than venous fenestrae in the intestine. They may allow large molecules to pass from the blood to the tissue more rapidly than they could via the slow system of endothelial vesicles[17,18], e.g. arterial fenestrae could provide corticotrophic hormones with rapid access to the gland cells. Since, however, arterial fenestrae are fewer than venous fenestrae, even with this efflux of molecules there could still be a net removal of large molecules from the tissue via these structures[2].

Résumé. Dans le cortex adrénal des souris les limbes des capillaries vieneux ont $\sim$4.3 fenestrae endothéliales de plus que les limbes artériels. On estime que cette prépondérance des fenestraes vieneuses, qui se retrouve ailleurs, et très importante et permet à celles-ci d'enlever du tissu les grandes molécules extravasculaires.

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Elektronenmikroskopischer Vergleich menschlicher Iriskapillaren bei Glaucoma simplex und bei Katarakt

Die Iriskapillaren von Menschen und Tieren sind von mehreren Autoren sowohl licht- als auch elektronenmikroskopisch untersucht worden[1–5]; dabei wurde auch ihre Wichtigkeit für die Augenphysiologie hervorgehoben. Mizuno[6] vertritt zum Beispiel die Auffassung, dass die Iriskapillaren bei der Produktion des Humor aquaeus eine Rolle spielen.

Material und Methoden. Mit der Absicht, die Ultrastruktur und den cytophysiologischen Zustand der Kapillarendothelzellen der menschlichen Iris bei erhöhtem intraokulärem Druck zu analysieren, haben wir intra operationem gewonnene Irisstückchen von fünf glaukomkranken Patienten (Glaucoma simplex) beiden Geschlechtes im Alter von 60–69 Jahren in 6,25%igem Glutaraldehyd vor-, dann in 1%igem OsO_4 nachfixiert und darauf in Araldit eingebettet. Zum Vergleich wurden Irisstückchen von einem männlichen und einem weiblichen Patienten der gleichen Altersklasse mit senilem Katarakt