ROLE OF THE VENULAR AND LYMPHATIC COMPONENTS OF THE MICROCIRCULATION IN TRANSCAPILLARY EXCHANGE IN ORGANS AT THE FUNCTIONAL UNIT LEVEL

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KEY WORDS: venular and lymphatic microvessels; permeability gradient; transcapillary exchange.

Transcapillary exchange of substances between the blood and tissue fluids takes place through the walls of arterial and venous capillaries, and the postcapillary venules occupy an important place in the mechanisms of tissue homeostasis at the level of functional units of organs [3]. The object of this investigation was to attempt, by the use of intravital contact luminescence microscopy, to shed light on some aspects of dynamic functional relations existing during normal transcapillary exchange between the venular and lymphatic microvessels of certain organs.

EXPERIMENTAL METHOD

Experiments were carried out on 28 male albino rats weighing 150-200 g. Superficial terminial microvessels of the mesentery, small intestine, and stomach were studied by the method of contact luminescence biomicroscopy suggested previously [2]. Special attention was paid to the state of vaso-tissue permeability of different parts of the microcirculatory bed of the organs chosen for study. Bovine albumin and globulin, labeled with fluorescein isothiocyanate (FITC), injected intravenously in a dose of 30 mg/100 g body weight, served as indicator of permeability.

EXPERIMENTAL RESULTS

The microcirculatory component of functional units of the organs studied is characterized by subdivision into different portions of the microvascular system (arterioles, capillaries, and venules) that are clearly distinguishable biomicroscopically. The results obtained point to the presence of a well-marked arteriolovenular permeability gradient in the above-mentioned organs, whereby the arteriolar portions and capillaries are impermeable to FITC-labeled albumin and globulin. Fluorescent proteins were found only in the lumen of those microvessels. Meanwhile the venular portions of the microvascular system were distinguished by high permeability for protein. Protein escaped from the postcapillary microvessels and small venules in the form of a fluorescent cloud (Fig. 1). Escape of protein into the interstices took place very rapidly, virtually immediately after its appearance in the lumen of the microvessel under the microscope. On leaving the postcapillaries the labeled protein was then reabsorbed by lymphatic microvessels, in which it appeared always later than in the blood vessels. These observations show that labeled protein is reabsorbed initially by the lymphatic microvessels located in the interstitial space in the immediate vicinity of the postcapillary venules (Fig. 2). Later, however, lymphatic microvessels topographically more remote from the point of initial capillaries containing reabsorbed protein could be distinguished particularly clearly, and the surface vessels of the small intestine became visible on biomicroscopy (Fig. 3). Besides in the lymphatic capillaries, fluorescent protein in the form of golden granules also was found in the endothelium of the venules (Fig. 2) and pericytes surrounding the venular segments. A noteworthy fact was that fluorescent granules in the endothelium and pericytes were distributed topographically only in those segments of the postcapillary vessels where extravasation of protein took place. These observations point to the presence of definite morphological and functional connections between the postcapillary venules, lymphatic microvessels, pericytes, and endothelial cells, that determine the composition of the protein profile of the interstitial fluid.

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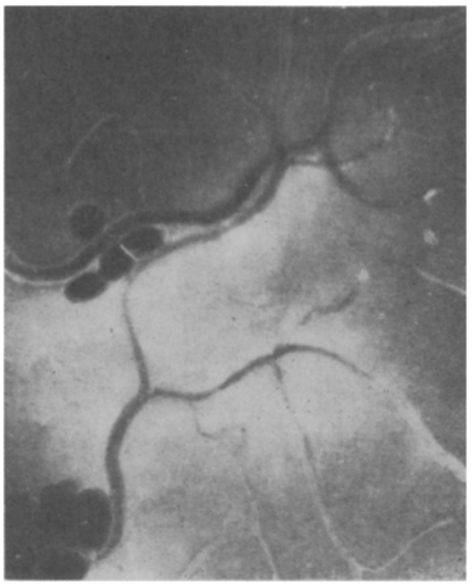

Fig. 1. Rat mesentery; 2 min after intravenous injection of bovine albumin labeled with FITC; extravasation of luminescent protein in region of venule. Here and in Figs. 2 and 3, contact luminescence biomicroscopy. Magnification 30 ×.

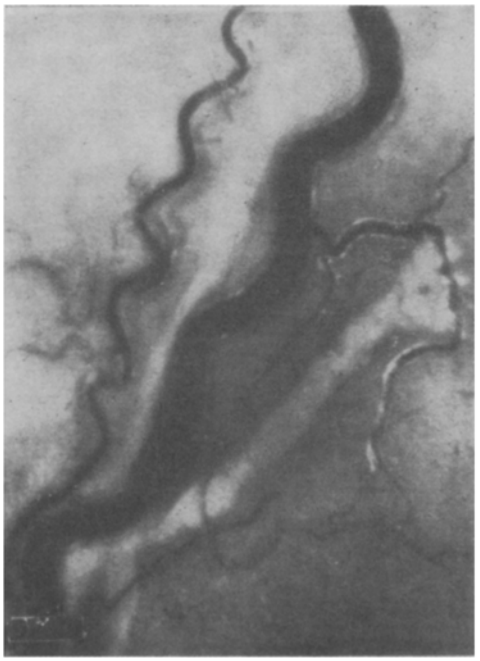

Fig. 2

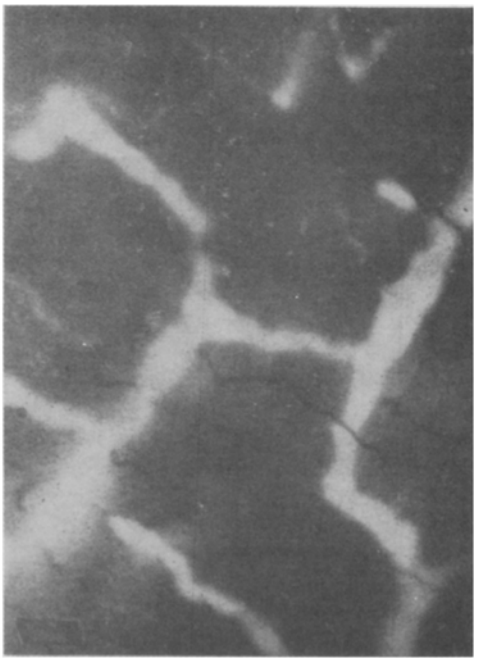

Fig. 3

Fig. 2. Mesentery of rat, 10 min after intravenous injection of FITC-labeled bovine globulin: luminescent granules of labeled protein visible in cytoplasm of endothelium of venules and also in lumen of two lymphatic microvessels running along venule.

Fig. 3. Small intestine of rat, 5 min after intravenous injection of FITC-labeled bovine globulin: superficial luminescent network of lymphatic microvessels can be seen.

It was shown previously that extravasation of protein also takes place in organs with a different structure of the vascular wall of their terminal microvessels (liver and kidney) [1]. Organs whose vascular wall differs in principle in its ultramicroscopic organization thus share a common phenomenon of extravasation of protein.

The biomicroscopic study of escape of protein through the wall of the microvessels, followed by the study of its fate in the extravascular space provide an interpretation of the

physiological role of this phenomenon as follows. The presence of physiological extravasation of protein at the level of the postcapillary and initial venular portions of the microvascular system increases the colloid-osmotic tissue pressure locally and increases the effective hydrostatic pressure within the vessel. This enables the postcapillaries and small venules to perform an exchange function instead of a drainage function, so that the effective vascular surface participating in filtration processes in the direction from blood to tissue can be considerably increased.

Meanwhile extravasation of protein in certain parts of the microcirculatory system with its subsequent reabsorption by lymphatic microvessels may be one of the mechanisms responsible for maintaining regional tissue equilibrium at the level of the functional unit of the organ under normal conditions. The modern concept of tissue equilibrium in the field of transcapillary exchange is based on a group of mechanisms established by Starling as long ago as in 1896, and subsequently confirmed and extended by the classical investigations of Iandis [3]. According to Starling's theory, the factors which establish and guarantee the fluid balance are filtration and reabsorption on account of the difference between hydrostatic and colloid-osmotic pressures at the arteriolar and venous ends of the capillary system. The following principles are postulated: the existence of uniform permeability and the geometric symmetry of the capillary network at the arteriolar and venous ends of the capillary bed [3], and the relative impermeability of the capillary wall for protein. However, a number of factors obtained comparatively recently do not fit into this concept and may even contradict it: The permeability of the venular segments of the terminal bed of the mesentery for low-molecular-weight compounds and water is 2-6 times higher than that of the arterial segments [6, 8, 10]; the vascular surface in the region of the postcapillary venules is 6 times larger than in the region of the arterial capillaries [9]; the capillary wall of certain organs can allow the passage of macromolecules [1, 3-5].

If Starling equilibrium between hydrostatic and colloid-osmotic pressures in the blood and tissue really exists for organs such as the mesentery, intestine, and stomach, the presence of high permeability of the venular segments and the large vascular surface of the postcapillary drainage microvessels would produce such powerful reabsorption of interstitial fluid that this would inevitably lead to dehydration of the tissues. However, the high permeability of the postcapillary vessels of the terminal bed with respect to protein can reduce the intravascular colloid-osmotic pressure locally. This, in turn, regulates the process of reabsorption of interstitial fluid in these segments and prevents dehydration of the tissues. Protein escaping from the postcapillaries is then reabsorbed by lymphatic microvessels. Pericytes and endothelial cells of the postcapillary venules also play a definite role in the control of the tissue oncotic pressure. A hemodynamic peculiarity of the microcirculation in the liver is the low velocity of the sinusoidal blood flow and low hydrostatic pressure. Establishment of regional tissue equilibrium of the Starling type is therefore possible provided that the transmural colloid-osmotic pressure also is low, and this is compatible only with high permeability of the sinusoid wall for protein molecules. In the kidneys the presence of physiological permeability of the capillaries for protein can modify the local ratio between hydrostatic and oncotic pressures dynamically, and thus serve as a factor maintaining glomerular–tubular balance at the single nephron level despite considerable fluctuations of pressure in the renal artery. The extravasated protein is then actively reabsorbed by the epithelium of the proximal tubules, broken down, and reutilized [1].

The passage of protein through the system of membrane formations of the microvascular wall of the above-mentioned organs under normal conditions thus becomes a fact which does not contradict Starling's concept, but which supplements it with respect to the realization of the filtration mechanism of permeability in organs differing in the structure of their microvascular wall. The results described above and their interpretation are in agreement with views developed in recent years by Hauck et al. [5-7].

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ULTRASTRUCTURE OF AXOSOMATIC JUNCTIONS ON NEURONS OF THE RAT SENSOMOTOR CORTEX AND CELIAC GANGLIA FROM THE AGE ASPECT

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KEY WORDS: cerebral cortex; celiac ganglia; synapses; aging.

There have been several investigations devoted to the ultrastructural analysis of development of the system of interneuronal synapses at different stages of ontogeny [4, 5, 11]. In some of them, besides qualitative data, quantitative information also is given on many parameters, but these are predominantly global in nature, covering all types of junctions and not allowing for the different layers of the cerebral cortex [2]. It seemed more rational to the authors to undertake a separate study of each system of interneuronal synapses (axodendritic, axosomatic, and so on) taking into account their topographic, structural, and functional differences. The quantitative ultrastructural characteristics of interneuronal synapses of the celiac ganglia have not previously been studied from the age aspect.

The object of this investigation was to study the qualitative and quantitative ultrastructural parameters of axosomatic junctions on pyramidal neurons in the cerebral cortex and on neurons of the celiac ganglia in noninbred albino rats aged 6 months (young) and 30 months (old).

EXPERIMENTAL METHOD

Pieces of tissue from the sensomotor cortex and ganglia of the celiac plexus from 30 rats were fixed in osmium tetroxide and embedded in Araldite. Sections were cut on UMTP-I and LKB-III microtomes and photographed on UÉMV-100B and JEM-7A electron microscopes. Axosomatic junctions were determined per unit length (10 μ) of perimeter of a pyramidal neuron in cortical layer V and on the perimeter of a ganglionic neuron. All data were obtained from 130 junctions on 90 neurons of the celiac ganglia and from 1450 junctions on 162 cortical neurons.

EXPERIMENTAL RESULTS

Previous investigations have shown that axosomatic junctions are not numerous on pyramidal neurons [2, 12] and are rare on neurons of sympathetic ganglia [3, 8, 13, 14]. Our observations showed that there are 3.70 ± 0.22 axosomatic junctions with a junction length of 0.85 ± 0.05 μ and with an area of axon of 0.53 ± 0.06 μ^2 per 10μ perimeter of a pyramidal neuron in young rats. The corresponding figures for old rats were 3.50 ± 0.23 and 0.94 ± 0.09 μ and 0.58 ± 0.08 μ^2. In the celiac ganglia of young rats there were 1.5 ± 0.44 axosomatic junctions per neuron and 2.35 ± 0.47 in old rats. The axon diameter was 0.58 ± 0.035 in the young rats and 0.77 ± 0.033 μ in the old.

Axons forming synapses were found mainly in transverse section (Figs. 2 and 4). These transverse profiles could belong to "en passant" terminals and to terminal axon expansions.

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