FORMATION OF REACTIVITY OF THE MESENTERIC MICROCIRCULATORY SYSTEM IN PUBERTAL RATS

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Reactivity of microvessels is one of their important morphological and functional characteristics, since responses of small arteries and large arterioles are under the direct influence of the nervous system, and an important role in regulation of the lumen of small arterioles and precapillaries is played by locally produced vasoactive substances [8, 14]. Among components of the microcirculatory system, it is the precapillaries and arterioles that are most reactive [15]. The morphological substrate for enhancement of the response of the precapillaries and arterioles is an increase in the number of myoepithelial junctions in the walls of the microvessels [12]. A change in reactivity of the microvessels reflects the state of the microcirculation and is an important prognostic sign in essential hypertension [7, 9], acute blood loss [4], and massive blood transfusion [6].

A particularly interesting aspect of solution of the problem of interconnection between function and structure in the microcirculatory system is the study of its reactivity during development. It is stated in [2, 5] that age transformations of pathways of the microcirculation with age are accompanied by corresponding changes in their reactivity. Stabilization of this parameter occurs near the time of formation of the definitive structure of the microcirculatory system.

The aim of the investigation described below was to study changes in reactivity of microvessels in the albino rat mesentery discovered in response to the action of adrenalin in the pubertal period, which is the time when the structure of the microcirculatory system is formed.

EXPERIMENTAL METHOD

Changes in reactivity of the mesenteric microvessels were studied in 90 rats at weekly intervals between the ages of 3 and 13 weeks. The animals were prepared for investigation and biomicroscopy of the small intestinal mesentery by methods described previously [3, 13]. To demonstrate the response of the microcirculatory system, local application of adrenalin solution was used. For this purpose a test scale of its dilutions from 100 to 0.01 μg/ml in physiological saline was prepared. Adrenalin solution was applied to the surface of the mesentery drop by drop in a volume of 0.1 ml. During biomicroscopy, the time at which the primary changes in blood flow (appearance of a granular flow of blood in the postcapillaries and venules) and the time of arrest of the blood flow (the so-called "stasis effect") were measured with a stopwatch. Sensitivity of the microvessels to adrenalin was measured as the reciprocal of the time of appearance of primary changes in the blood flow. In addition, during biomicroscopy the number of arterioles and venules in the segment was counted and the diameter of the microvessels measured.

EXPERIMENTAL RESULTS

Formation of the microcirculatory system in individual segments of the rat mesentery usually begins the the 3rd week of postnatal life. This is expressed by the appearance of single arteriolo-venular loops, in the middle part of which a capillary link can be distinguished. During development, by the 5th-7th week the number of arterioles and venules per

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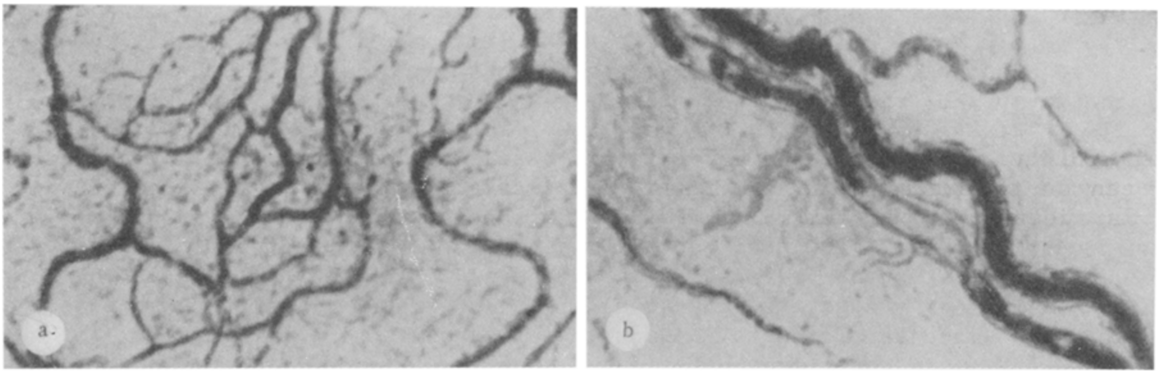

Fig. 1. Primary changes in blood flow in capillaries and venules after application of adrenalin (a) and the "stasis effect" (b). Objective 16, ocular 7.

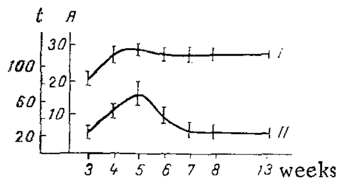

Fig. 2

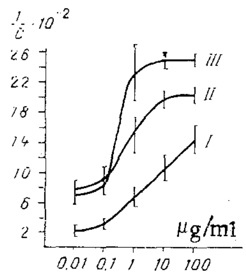

Fig. 3

Fig. 2. Changes in diameter of arterioles and time of arrest of blood flow during application of adrenalin in a concentration of 1 μg/ml. Abscissa, age of animals (in weeks); ordinate: A) diameter of arterioles (in μ), t) time of arrest of blood flow (in sec). I) Changes in diameter of arterioles, II) changes in time of response.

Fig. 3. Stages of formation of reactivity of mesenteric microcirculatory system during development. Abscissa, adrenalin concentration (in μg/ml); ordinate, sensitivity of microvessels (in $1/C \cdot 10^{-2}$). I) Early stage (3-5 weeks), II) intermediate stage (7-8 weeks), III) mature stage (after 13 weeks).

segment increases, as also does their diameter, and ramifications of the capillary network are formed. With age the diameter of the capillaries falls from 12 to 7.5 μ. The largest number of growing capillaries was found in the mesentery of rats aged 5 weeks. The definitive structure of the mesenteric microcirculatory system was formed by the 13th week of development of the rats.

Changes in blood flow in the mesenteric microvessels in response to local application of adrenalin solution were similar in direction at all stages of development. Two phases of changes in circulation of the blood could be distinguished. In phase I a slow, granular blood flow was observed with the appearance of small aggregates of cells in the capillaries, postcapillaries, and venules (Fig. 1a). In phase II marked intravascular aggregation of erythrocytes was observed in all parts of the microcirculatory system, with arrest of the blood flow (Fig. 1b). This response of the blood flow was due mainly to constriction of arterioles 28-32 μ in diameter.

At all stages of age development studied the time of the response of the microvessels was directly dependent on adrenalin concentration, as was most evident between values of 0.01 and 0.1 μg/ml. Higher adrenalin concentrations caused rapid arrest of the blood flow followed by development of signs of stasis. The data in Fig. 2 show that the time of arrest of the blood flow during application of adrenalin solutions of identical concentration varied with age. The onset of the response of the microvessels took place more slowly in animals aged 3-5 weeks. These results correlate quite satisfactorily with changes in structural parameters (in particular, the diameter of the arterioles). After the 5th week the response of the microvessels was accelerated, and after the 7th week it became stabilized. Acceleration of the response between the ages of 5 and 7 weeks may be attributed to the fact that during formation of the arteriolar wall there is an increase in contractility of the smooth muscle cells. This is supported by the results of investigations [1, 10, 11] which revealed gradual strengthening of contractile function of the smooth muscle cells in the blood vessel walls in ontogeny due to an increase in the number of intermuscular junctions. Another important fact is evidently that this period of development of the microcirulatory system is characterized by intensive growth of capillaries and their inclusion in the circulation. This brings about the formation of precapillary sphincters, which are known [15] to be most sensitive to the action of vasoactive substances. The appearance of components of the microcirculatory system more sensitive to vasoactive substances during ontogeny may perhaps be responsible for the more rapid manifestations of the response of the microvessels. Relative stabilization of microvascular reactivity observed after the age of 7 weeks corresponds in time to formation of the definitive structure of the mesenteric microcirulatory system.

During development not only is the level of sensitivity of the microvessels raised, but the character of their response also changes. These results enable three stages of formation of mesenteric microvascular reactivity to be distinguished (Fig. 3). In the initial period of development (3-5 weeks) sensitivity of the microvessels rises gradually with an increase in concentration of the adrenalin solution. At the age of 7-8 weeks the character of the microvascular response changes: The response occurs more rapidly as the adrenalin concentration is increased from 0.1 to 10 μg/ml. Finally, in animals aged 13 weeks there is a jump of threshold sensitivity within an even narrower range of concentrations (0.1-1 μg/ml), coupled with development of the definitive structure of the microcirculatory system. It can accordingly be concluded that stages of formation of reactivity of the mesenteric microcirculatory system during ontogeny are connected with the formation of the structure of the microvascular bed.

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