# MICROCIRCULATION AND PERMEABILITY OF THE PULMONARY CAPILLARIES IN THE COURSE OF EXPERIMENTAL VAGUS NEURITIS

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The trophic function of the nervous system and dystrophies of nervous origin still constitute an important problem in experimental medicine. To study this problem the method of artificial disturbance of connections between the CNS and an innervated organ is usually used. It was shown previously [5] that vagus nerve stimulation leads to the development of pulmonary edema and pneumonia, and this is evidently connected with a disturbance of the pulmonary hemodynamics and changes in permeability of the pulmonary capillaries.

The object of the present investigation was to study changes in permeability and the microcirculation of the pulmonary capillaries in the course of experimental vagus neuritis, by the use of intravital biomicroscopy [3].

## EXPERIMENTAL METHOD

Experiments were carried out on 210 noninbred albino rats weighing 180-220 g. Neuritis of the right vagus nerve was induced in one group of animals (140 rats) [5]. In this case turpentine was not injected into the nerve trunk, but a ligature soaked in turpentine was applied directly to the nerve in its cervical portion. The second group of intact animals (70 rats) served as the control. Biomicroscopy of the pulmonary artery was carried out daily for 14 days after application of the ligature to the nerve. The technique suggested previously [3] was used. Disturbance of vascular permeability was determined by an ink method [1, 6, 11]. For this purpose, 0.2 ml of a 0.1% solution of India ink, filtered first through a No. 4 glass filter and warmed to 38°C, was injected into the femoral vein of animals of both groups. Particles of ink were counted 30 min after injection, for according to data in the literature at the end of this period ink is found in normal animals in the reticuloendothelial system, liver, spleen, and lymph nodes [1]. The number of visually detectable ink particles adherent to the endothelium of the lung capillaries was counted in seven fields of vision (magnification 950 ×), the total area of which, according to instructions with the MBI-15U microscope, was 0.1 $mm^2$. Biomicroscopy was carried out on the same regions in the center of the middle lobe of the right lung. To avoid re-examination of the same region of lung tissue, and also to confirm stable adhesion of the ink particles to the capillary endothelium, visual observation was supplemented by photographic recording. The time of observation of one visual field was 30 min. The diameter of the pulmonary microvessels was determined during inspiration, under constant magnification of the microscope by 380 times. The numerical data for these parameters were obtained by analysis of previously exposed motion picture film on a mounting stage with superposed micrometer scale. For the same purpose, serially exposed photographic negatives (at intervals of 15 sec for 2-3 min) were projected with a photographic enlarger on a micrometer scale [7]. The state of the hemodynamics was assessed on the basis of visual observation and also of still and motion picture photography.

## EXPERIMENTAL RESULTS

In the groups of control animals the adhesive power of the capillary endothelium relative to ink showed no significant change over a period of 14 days and averaged 8.9 ± 0.3 ink par-

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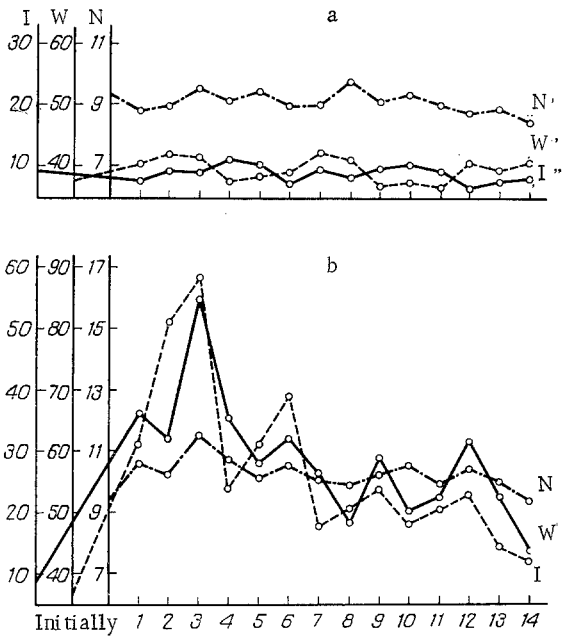


Fig. 1. Number of ink particles adherent to capillary endothelium and change in diameter of capillaries in the course of experimental vagus neuritis. Abscissa, time (in days); ordinate: I) number of adherent ink particles, W) wide capillaries (in μ), N) narrow capillaries (in μ); a) control, b) experiment.

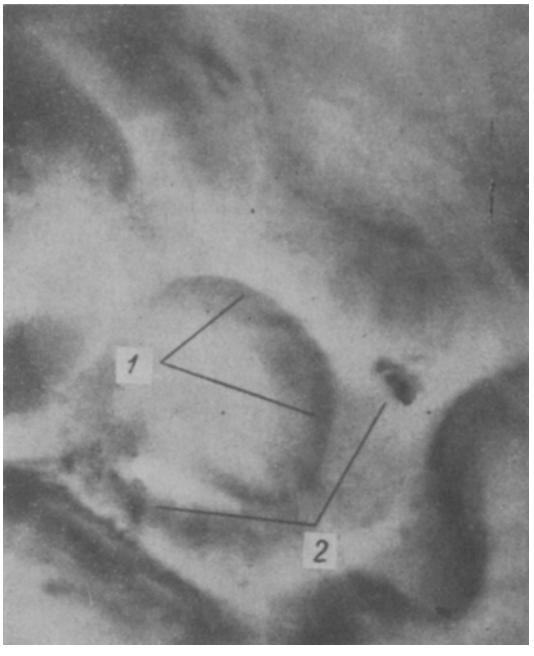


Fig. 2. Adhesion of ink particles in pulmonary capillaries (× 380). 1) Lung capillaries, 2) ink particles.

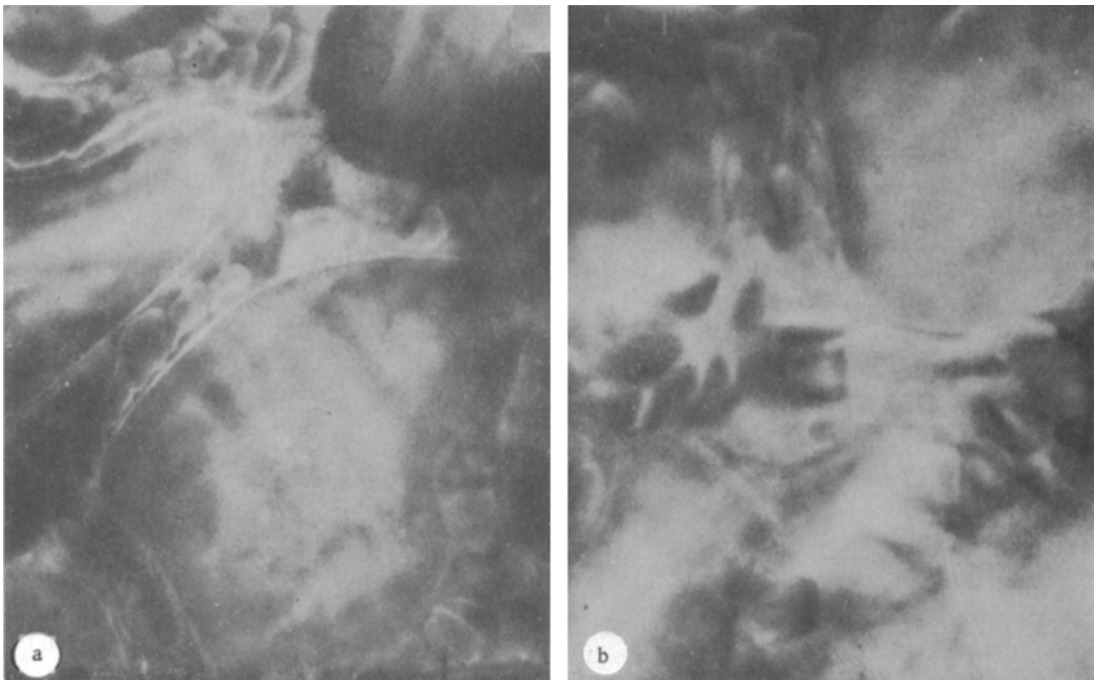

Fig. 3. Narrow lung capillaries (× 380). a) Intact animal, b) on 3rd day after application of turpentine to nerve.

ticles/0.1 mm$^2$. The diameter of the microvessels likewise did not change significantly. The mean diameter of "narrow" capillaries was 9.2 ± 0.1 μ, and of "wide" 36.4 ± 0.8 μ (Fig. 1a). The hemodynamics was constant in character [2]. It was a different matter in the group of animals with experimental neuritis of the vagus nerve (Fig. 1b). In this case, the number of adherent ink particles on the day after application of the ligature already averaged 35.1 ± 3.6, significantly ($P < 0.001$) higher than in the control group. The maximal number of adherent ink particles was observed on the 3rd day after application of the ligature, when it was 55.6 ± 3.8, significantly ($P < 0.001$) higher than the corresponding parameter in the control group and during the previous days (Fig. 2). On the following days the adhesive power of the endothelium was phasic in character, increasing threefold every third day (Fig. 1b), namely on the 3rd, 6th, 9th, and 12th days.

The adhesive power of the capillary endothelium at these times was significantly higher than that of the endothelium on previous days.

The diameter of the microvessels also changed significantly (Fig. 3). On the day after stimulation of the vagus nerve there was already a significant increase in diameter of both types of capillaries, which reached its maximum on the 3rd day (Fig. 1b). Dilatation of the microvessels could be noted for all 14 days. In most cases the maximum of dilatation corresponded to the maximum of increase in adhesive power of the capillary endothelium (Fig. 1b).

Considerable changes also were found in the hemodynamics. For instance, whereas in the control group of animals no signs of stasis, of to-and-fro movements of blood, were observed, in the experimental group this was found quite often. This was particularly marked on the 3rd, 6th, 9th, and 12th days after application of the ligature. Signs of stasis were found in some areas of lung tissue from 2 to 30 min or more. To-and-fro movement of blood was observed in the capillaries for between 1 and 10 min.

Electron-microscopic studies in recent years have shown that the increase in microvascular permeability is characterized by the formation of spaces between adjacent endothelial cells [4, 8, 9, 10]. It can accordingly be suggested that accumulation of ink particles in the pulmonary capillaries is due to the presence of these spaces in this particular pathological process. The results of the investigations described above thus showed that disturbance of nervous regulation is substantially reflected in the hemodynamics and vascular permeability of the lung capillaries. It was found in these experiments that these disturbances are synchronized in time and in the intensity of their manifestations, and that they are phasic in character.

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# PREVENTION OF POSTRESUSCITATION HEART FAILURE WITH IONOL

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Activation of lipid peroxidation (LPO) in heart muscle is observed in emotional-painful stress [9], hypoxia, and reoxygenation [8, 16]. Together with activation of phospholipases and the detergent action of an excess of fatty acids [13], this process plays an important role in the mechanism of injury to the lipid bilayer of the cardiomyocyte membranes and disturbances of cardiac function in these states. The mechanism of disturbances of the contractile function of the heart observed during resuscitation after clinical death [6, 10], is not clear. Since stress, hypoxia, and reoxygenation are observed in various combinations in the course of this process, it can be tentatively suggested that LPO activation and injury to the membrane apparatus of the cardiomyocytes both play a role in postresuscitation heart failure.

To test this hypothesis, in the investigation described below LPO activity and the contractile function of the heart were studied in animals during resuscitation after clinical death, after which an attempt was made to prevent the disturbances of contractile function thus revealed by means of the synthetic antioxidant ionol (2,6-di-tert-butyl-4-methylphenol).

## EXPERIMENTAL METHOD

Experiments were carried out on male rats weighing 190-220 g anesthetized with pentobarbital (25 mg/kg). There are four series of experiments: I) control animals; II) animals resuscitated from clinical death; III) animals receiving ionol; IV) animals receiving ionol before clinical death. Each group contained 10 or 11 animals. Clinical death, for a duration of 4 min, was induced by acute bleeding through the carotid artery, and the animals were resuscitated by centripetal injection of the lost blood and artificial ventilation of the lungs. Ionol was injected intraperitoneally in a dose of 100 mg/kg daily for 3 days. For biochemical tests and for the study of its contractile function the heart was removed 6 h after resuscitation. Lipids were extracted from the myocardium by the method in [15]. Accumu-

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