preference by rats for salt solution may be similar to the antidipsogenic effect of substance P and may be effected through modulation of taste perception as a result of a change in monoamine and GABA metabolism. Intensification of the attraction for salt, under the influence of a procedure aimed at lowering the endogenous peptide level in immunized rats, indicates the important role of the bombesin-like factor in the "salt appetite." The fact that immunocorrection is a long-lasting effect is of definite interest. The data described in this paper are thus an example of the possibilities of long-term changes in physiological functions by immunization against biological regulators.

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PULMONARY MICROCIRCULATION DURING ARTIFICIAL VENTILATION WITH DIFFERENT FREQUENCY AND VOLUME PARAMETERS

A. M. Kulik, S. B. Tkachenko, and V. G. Nikulin

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Artificial ventilation of the lungs (AVL) is widely used in clinical practice to treat patients with acute respiratory failure [2, 3, 5]. The effect of AVL on the microcirculation of the lungs has received little study. Some research has been carried out in this direction but under open chest conditions, and on isolated or quickly frozen lungs [1, 9, 12], and their results may therefore differ significantly from changes in the pulmonary circulation during AVL in animals with a closed chest. Research in which the state of the microcirculation during AVL was judged by the hematocrit index in pulmonary capillaries, the vascular resistance in the pulmonary circulation, the respiratory quotient, and other indirect parameters [1, 8, 10], was uninformative.

The aim of this investigation was to study changes in the diameter of arterioles, venules, and wide capillaries and in the length of functioning narrow capillaries, during AVL with different frequency and volume parameters on animals with a closed chest.

Laboratory of Pathophysiology of Respiration and Laboratory of Experimental Pathomorphology, Research Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow.

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TABLE 1. Effect of Increased Frequencies and Volumes of AVL Schedules on Changes in D_w, D_a, D_v, and N

AVL schedule	D_w	D_a	D_v	N
	M			
Control	13,2±0,9	32,3±3,2	17,4±1,9	246,1±24,6
Two fold increase in frequency	10,8±0,7*	26,5±2,9	13,7±2,9	132,3±13,2**
Control	14,0±0,9	27,7±3,4	17,4±2,1	285,3±32,0
Threefold increase in frequency	10,9±0,8*	24,3±3,4	14,8±1,9	166,9±24,8**
Control	14,3±0,5	20,3±2,5	28,1±2,9	243,5±34,1
1.5-Fold increase in volume	11,0±0,7**	16,1±2,8	24,3±2,7	156,6±24,5*
Control	13,4±0,7	21,1±2,5	26,8±2,2	249,7±25,5
Twofold increase in volume	9,9±0,4**	15,9±1,7	23,5±2,4	154,5±26,1*

Legend. *$p < 0.05$, **$p < 0.01$; significance of differences compared with control.

EXPERIMENTAL METHOD

The experiments were carried out on 30 cats weighing 2.5-4 kg anesthetized by intraperitoneal injection of pentobarbital (30-40 mg/kg). The pulmonary microcirculation was studied by contact biomicroscopy [4]. Subpleural zones of the upper lobe of the right lung were investigated. To exclude active respiratory movements the animal was immobilized by intravenous injection of tubocurarine (initial dose 0.5 mg/kg, followed by a further 0.25 mg/kg on the appearance of evidence of a return to spontaneous respiration). The "Vita-1" variable volume-frequency respirator was used for AVL. The initial parameters of AVL corresponded to the volume (RV) and frequency (RR) of the animal's natural breathing. Each new AVL schedule was used for 3-5 min, and an interval of 10 min was allowed between schedules. The blood pressure in the femoral artery (BP) was recorded by a mercury manometer and the intratracheal pressure (ITP) was measured by an air manometer. A constant pressure (between −70 and −90 mm water) was maintained in the pleural cavity by means of a vacuum pump. The blood gas composition was determined by the Astrup–Siggard–Andersen micromethod. During the experiment pictures of the test region of the lung were recorded by video recorder from a television screen. The diameter of the arterioles (D_a), venules (D_v), and wide capillaries (D_w) and the length of the functioning narrow capillaries (N) were measured by means of an ASM semiautomatic image analyzer ("Leitz, West Germany) [6, 7]. All measurements of the parameters of the microcirculatory bed of the lungs chosen for study were made at expiration. The results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

AVL at constant volume but with double the frequency caused a reduction of D_w by 18% and N by 46% in all the animals tested. If the frequency of AVL was trebled, D_w was reduced by 22% and N by 43%. In about 50% of alveoli studied, without blood flow in their narrow capillaries during initial ventilation, a two- and threefold increase in the frequency of AVL led to the appearance of individual functioning capillaries. D_a and D_v had a tendency to fall by 18 and 22%, respectively, in response to twice, and by 12 and 15% in response to 3 times the initial RR. ITP at inspiration rose as a linear function from 8 to 20 cm water and corresponded to the degree of increase in RR. An increase in RV by 1.5 times, with constant frequency of AVL, also led to a decrease in D_w in all cases by 23% and in N by 36%. With a twofold increase in the volume of AVL D_w was reduced by about the same amount (26%), and the same also was observed with N (by 38%). Alveoli with nonfunctioning narrow capillaries during artificial ventilation, in which a blood flow appeared in response to an increase in the volumes of AVL by 1.5 and 2 times, accounted for about 25% of the

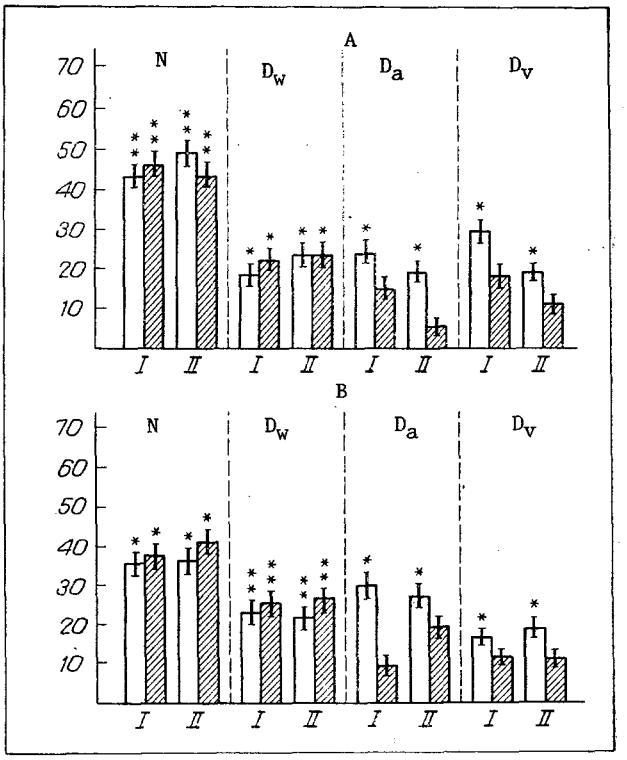

Fig. 1. Changes in diameter of arterioles (D_a) and venules (D_v), in D_w, and in length of functioning narrow capillaries (N) depending on their initial values during AVL with increased frequencies or volumes. A) Increased frequency schedules (I – twofold, II – threefold); B) increased volume schedules (I – 1.5-fold, II – twofold); ordinate, decrease (in %): N: unshaded columns – 100-332 μ, shaded – 332-564 μ; D_w: unshaded columns – 10-18 μ, shaded – 18-26 μ; D_a and D_v: unshaded columns – 13-33 μ, shaded – 33-54 μ). *$p < 0.05$, **$p < 0.01$ compared with control.

total. D_a and D_v were reduced by 21 and 13% in response to an increase in RV by 1.5 times and by 25 and 12% in response to a twofold increase in volume. Despite the linear nature of the rise of ITP at inspiration from 8 to 30 cm water in response to ventilation with increased volumes, the decrease in D_w, D_a, D_v, and N was nonlinear. During the period when AVL was used on a frequency or volume schedule, BP changed within the limits of error of the method. A threefold increase in the frequency of AVL led to reduction of pCO_2 of the arterial blood from 32.5 ± 1.4 mm Hg (pH 7.37 ± 0.03) to 24.5 ± 2.2 mm Hg (pH 7.48 ± 0.05), and a twofold increase in the volume led to reduction to 23.1 ± 1.2 mm Hg (pH 7.50 ± 0.03). Consequently, the use of the maximal increases in the frequency or volume of AVL used in these invetigations induced an equal degree of gaseous alkalosis in the animals.

The results show that an increase in both frequency and volume of AVL causes a decrease in N, D_a, D_v, and D_w. In the narrow capillaries, which did not function with the initial parameters of AVL, an increase of ventilation led to the appearance of a blood flow. With an increase in the frequency of AVL this phenomenon was observed twice as often as with an increase in its volume.

Reduction of the volume of AVL by half, while maintaining constant frequency, led to an increase in D_w on average by 22%. Changes in D_a, D_v, and also N in different parts of the test zone of the lung differed in magnitude: in 75% of the alveoli studied N was reduced by 32% and in the rest it was increased by 25%. In 75% of observations D_a was reduced by 22% and in the rest it was increased by 14%. In 67% of cases D_v was reduced by 17% and in 33% it was increased by 7%. ITP at inspiration fell from 8 to 3 cm water. Changes in BP during AVL with reduced volume were within the limits of error of the method.

Consequently, with a decrease in the volume of AVL D_w constantly was increased. D_a, D_v, and N could be either reduced or increased.

With an increase in the frequency or volume of AVL there was an increase in the tracheal and, consequently, in the alveolar pressure also, at inspiration [10]. The alveolar pressure in the lungs is one factor which affects the level of pressure in the microvessels, and, consequently, their diameter. An increase in alveolar pressure at inspiration in these investigations in response to an increase in ventilation led to a decrease in D_a, D_v, D_w, and N. However, since the relationship between changes in the parameters of the microvessels and the rise of alveolar pressure is nonlinear in character, and the degree of these changes differs in different parts of the lung, it can be tentatively suggested that other factors also are involved in the realization of these changes. Thus a fall of pCO_2 and a shift of the blood pH toward alkalosis in response to an increase in the frequency or volume of AVL may have a dilator action on the lung vessels. During stretching of the lung tissue, prostaglandins of the E group could be released from it, lowering the tone of the pulmonary vessels [11]. The results and data in the literature [13] are evidence that the use of AVL with reduced volume increases the inequality of perfusion of different parts of the lung. In areas of hypoventilation the blood flow is reduced as a result of the development of hypoxic and hypercapnic vasoconstriction in them, and in turn, this limits or may even arrest the blood flow in the vessels of these alveoli, and direct it into other groups of alveoli. However, this redistribution of the blood flow during AVL with reduced volume in the present investigations did not lead to adequate oxygenation of the arterial blood, as shown by a fall of pO_2 from 96.2 ± 3.6 to 65.1 ± 3.1 mm Hg. The absence of changes in BP with an increase or decrease in ventilation shows that baroreflexes from the vessels did not play a role in the realization of these changes.

Because of the great scatter of the changes in the values of the microvascular parameters in different parts of the lungs in response to an increase in the frequency or volume of artificial ventilation, the question arose whether the degree of the changes in D_a, D_v, D_w, and N depended on their initial values. To answer this question, the microvascular parameters were divided into groups depending on their initial levels. When AVL with increased frequencies or volumes was used, this parameter fell by an equal degree in alveoli with N equal to 100-332 μ and 332-564 μ. No differences likewise were observed in narrowing of the wide capillaries 10-18 and 18-26 μ in diameter during ventilation with the above schedules. However, arterioles and venules 13-33 μ in diameter were more strongly contracted than vessels 33-54 μ in diameter when AVL was used with either increased frequencies or increased volumes (Fig. 1). The results, in relation to arterioles and venules, confirmed the view [3, 9] that with an increase in alveolar pressure the diameters of the pulmonary vessels changed differently, depending on their initial values.

Thus the wide scatter of changes in the values D_a and D_v during AVL with increased frequency or volume can be explained by the different degrees of their constriction, depending on their initial diameter. As regards N and D_w, no such rule was discovered.

It can be concluded from the results that the use of AVL with increased frequency or volume leads to constriction of the arterioles and venules, to a degree which depends on their initial diameter, and also to a reduction of N and D_w. The value of N was changed by a greater degree in response to an increase of frequency, D_w to an increase in the volume of AVL. With a decrease in the volume of AVL changes in D_a, D_v, and N differed in direction in different parts of the lungs. The nonlinearity of changes in the microvascular parameters in response to an increase in ITP, and also the fact that changes in D_w and N did not depend on their initial values when AVL was applied with increased frequencies or volumes, is evidence that not only the alveolar pressure, but also other neurohumoral factors, are involved in the mechanism of the changes described above, and their influence requires further study.

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EXCITATION-CONTRACTION COUPLING IN FEMORAL ARTERIAL SMOOTH MUSCLE IN RESPONSE TO NORADRENALIN

A. V. Gurkovskaya and N. I. Gokina

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KEY WORDS: noradrenalin; femoral artery; smooth-muscle cells; contractions.

Noradrenalin (NA) causes contraction of smooth-muscle cells (SMC) of the femoral artery. The contractile response of the rat [5, 9, 13] and dog [8] femoral artery has been shown to be dose-dependent on NA, the excitatory effect of which is mediated through both α_1- and α_2-adrenoreceptors [8-10].

The aim of this investigation was to study the mechanism of the excitatory action of NA on SMC of the femoral artery and the ways by which the calcium ions involved in activation of contraction enter SMC.

EXPERIMENTAL METHOD

Experiments were carried out on spiral strips (about 0.5 mm wide) of the rabbit femoral artery, using a modified single sucrose gap method [1]. Contractile activity of the muscle strips was recorded under near-isometric conditions by means of a mechanotron. Electrical potentials and contractile activity were recorded simultaneously on graph paper tape by a KSP-4 instrument and also photographically from an oscilloscope screen. The composition of the Krebs' solution was as follows (in mM): NaCl – 120, KCl – 5.9, $NaHCO_3$ – 15.5, NaH_2PO_4 – 1.2, $MgCl_2$ – 1.2, $CaCl_2$ – 2.5, glucose – 11.5. EGTA (1 mM) and $MgCl_2$ (6 mM) were added to the calcium-free Krebs' solution. The temperature of the Krebs' solution was maintained at 36°C and its pH at 7.4. Numerical values are given as the mean ± σ (σ – standard deviation); n denotes the number of observations.

EXPERIMENTAL RESULTS

In concentrations of 5×10^{-8}-10^{-5} M, NA induced dose-dependent contraction of the muscle strips of the femoral artery (Fig. 1a). The mean effective dose of NA (ED_{50}) was 10^{-7} M, almost an order of magnitude higher than for SMC of the rat femoral artery [9]. A weak tonic contraction induced by NA in a concentration of 5×10^{-8} M was not accompanied by any marked change of membrane potential, but in a concentration of 10^{-7} M, NA induced membrane depolarization to 3 mV and a marked increase in tonic contraction (Fig. 1b) compared with the previous concentration. The response of the muscle strip to NA in a concentration of 5×10^{-7} M is shown in Fig. 1c. Often against the background of depolarization, when it reached 5 mV, action potentials (AP) appeared, accompanied by phasic contractions,

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