It can thus be concluded from the results of this investigation that disturbances of ventilation of the lungs accompanying gravitatinal atelectasis are mixed restrictive-obstructive in nature. For the objective diagnosis of these disturbances, besides traditional spirographic methods, determination of the expiratory airway closure can provide significant information for it can bring to light early obstructive disturbances of lung ventilation and it allows the dynamics of recovery of this function to be studied.

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EXPERIMENTAL ACUTE HIGH ALTITUDE PULMONARY EDEMA AND THE MECHANISMS OF ITS DEVELOPMENT

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KEY WORDS: acute high-altitude pulmonary edema; oxygen saturation of arterial blood; circulating blood volume.

The syndrome of acute high-altitude pulmonary edema (AHAPE) is frequently found in the mountainous regions of our planet [2, 4-12, 14, 16]. However, the causes and mechanisms of its development have not yet been explained. The prevention of the syndrome is still less near to solution. The difference of opinion on the origin and mechanisms of development of the AHAPE syndrome can be explained by the absence of an experimental model of the syndrome in animals that corresponds adequately to the natural condition, so that the development of its various phases could be reproduced in order to discover the importance of disturbances of the various functional systems in this process and the order in which they come into operation.

The object of this investigation was to determine the possible mechanisms of development of the AHAPE syndrome.

EXPERIMENTAL METHODS

Experiments were carried out on 60 male chinchilla rabbits weighing 2.9-4.5 kg. The animals were kept in a clinical pressure chamber at an "altitude" of 6 km, where the meteorologic factors (temperature, wind velicity, air humidity, UV irradiation) corresponding to that altitude were reproduced. Under these conditions the various parameters chosen for study were determined every hour for 360 min. To assess the functional state of the cardiovascular system the ECF was recorded in standard lead II on a 6NEK-401 apparatus and the great vessels and chambers of the heart were catheterized for recording of the pressure curves

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TABLE 1. Changes in Respiration in Animals at a "High Altitude" (M ± m)

Parameters	Initial	Time, min					
		60	120	180	240	300	360
Respiration rate, cycles/min	119,4	144,2	147,7	148,3	151,2	151,2	152,2
	14,9	17,9	18,5	22,7	21,9	18,2	17,9
RMV, ml	652,5	795,5	820,7	826,0	791,2	752,2	729,0
	93,6	99,1	93,3	104,1	120,8	104,2	104,4
Oxygen concentration in expired air, vol. %	17,1	16,8	16,9	17,0	17,4	17,8	18,3
	0,27	0,3	0,3	0,4	0,3	0,3	0,4
Oxygen concentration in alveolar air, vol. %	15,6	15,5	15,5	15,3	15,3	15,8	16,4
	0,4	0,4	0,4	0,5	0,6	0,6	0,5
Oxygen saturation of arterial blood, vol. %	95,6	69,1	65,7	66,6	61,6	49,8	39,9
	1,76	3,5	6,0	5,8	5,8	4,4	3,0
Tidal air, ml	5,56	5,63	5,67	5,72	5,38	5,06	4,86
	0,98	0,96	0,94	1,14	1,17	0,88	0,80
Physiological respiratory dead space, ml	1,51	1,31	1,43	1,77	1,96	1,94	1,97
	0,45	0,47	0,49	0,69	0,68	0,46	0,42
Alveolar ventilation, ml/min	500,0	556,6	596,9	546,4	451,4	397,4	350,3
	68,5	80,5	86,1	87,5	90,2	70,0	61,1
Ratio of alveolar to pulmonary ventilation	0,72	0,76	0,75	0,69	0,64	0,61	0,59
	0,06	0,08	0,07	0,08	0,08	0,07	0,05
Arteriovenous oxygen difference, vol. %	2,69	0,65	0,66	0,64	0,57	0,51	0,46
	0,34	0,07	0,06	0,07	0,08	0,08	0,08
Intensity of oxygen uptake, ml/min/m	52,9	14,7	15,1	14,5	12,7	10,6	8,9
	8,15	1,72	1,49	1,93	1,76	1,69	1,59

TABLE 2. Changes in Circulation in Animals with AHAPE Syndrome (M ± m)

Parameters	Time, min						
	initial	60	120	180	240	300	360
Heart rate, beats/min	203	232,0	232,3	231,0	231,2	227,8	226,0
	22,0	28,3	26,9	26,6	23,8	20,5	18,0
Systolic pressure, mm Hg	102,5	111,2	113,8	110,4	104,6	99,9	96,2
	4,4	3,7	5,2	7,7	9,3	4,8	4,4
Diastolic pressure, mm Hg	65,0	65,5	63,3	69,0	70,7	71,8	73,7
	5,8	5,13	5,8	7,2	7,1	4,6	5,48
Cardiac output, ml/min	677,7	778,0	789,7	778,5	711,0	716,2	677,5
	97,3	114,3	111,6	103,8	104,3	110,0	114,7
Blood ejection time from left ventricle	0,08	0,07	0,071	0,072	0,073	0,078	0,079
	0,008	0,009	0,007	0,007	0,006	0,007	0,007
Mean dynamic pressure, mm Hg	77,5	80,7	80,2	82,8	82,0	80,1	81,2
	4,9	4,0	4,6	5,5	6,0	3,8	4,7
Cardiac index, liters/m^2	1,96	2,25	2,29	2,26	2,24	2,07	1,96
	0,13	0,19	0,17	0,16	0,15	0,15	0,18
Total peripheral resistance	10 044	9238	9106	9322	9215	9750	60 251
	1 494	1325	1265	1115	1272	1594	1 677
Velocity of blood flow	3,46	3,0	3,2	3,1	3,72	4,41	5,26
	0,31	0,27	0,24	0,30	0,36	0,35	0,47
Total pulmonary resistance	572	896	781	1016	1440	1650	1731,0
	68,0	110,6	84,7	69,8	109,4	132,3	120,0

by Mingograph-81 electromanometers (from Elema, Sweden). The cardiac output and central blood volume were determined and the velocity of the blood flow from the right heart to the ear and the circulating blood mass were measured by a dye method. The permeability of the pulmonary vessels was determined by measuring the outflow of dye into the lung tissue. Disturbances of gas exchange were judged on the basis of the following parameters: the respiratory minute volume, respiration rate, quantity of absorbed oxygen, concentrations of carbon dioxide and oxygen in samples of expired alveolar air and inspired air, and the oxygen saturation of the arterial blood. On the basis of these measurements parameters of the oxygen regime of the animal and their efficiency were calculated [1]. The acid–base balance of the blood was determined on a micro-Astrup apparatus (from Radiometer, Denmark). In the course. of the experiment the concentrations of catecholamines and of sodium and potassium ions were determined in the blood plasma and lung tissue. After exposure of the animals for 6 h they were killed and preparations obtained from their lung tissue for morphological diagnosis of AHAPE. The diagonsis of AHAPE was confirmed by determination of the lung coefficient and the dry residue of the lungs [3]. The numerical data were subjected to statistical analysis by EC-1020 computer.

EXPERIMENTAL RESULTS

As the oxygen saturation of the arterial blood fell at a high "altitude" the function of the respiratory and circulatory organs was activated. The increase in respiratory minute volume was due to an increase not only in the frequency of the respiratory movements, but also of their depth. This was shown by the increase in the tidal air during the first few hours of exposure of the animals and a decrease in the physiological respiratory dead space, as a result of which the elimination of CO_2 was enhanced and the oxygen concentration in the alveolar air was increased. All these disturbances contributed to the final effect of intensification of external respiration: maintenance of a satisfactory level of oxygen saturation of the blood in the lung capillaries.

That the efficiency of external respiration was adequate during the first hours of ascent to a high altitude is also shown by the ratio of the alveolar to pulmonary ventilation (Table 1). Parallel with this, changes were observed in the circulatory parameters. The systolic pressure and velocity of the blood flow were increased. All these measures are aimed at improving the oxygen supply to the tissues. The blood ejection time from the left ventricle and the power index of myocardial contraction were reduced.

All these initial shifts gradually disappeared by the 180th minute of the experiment and after the 240th minute the various parameters moved in the opposite direction. Phase analysis of activity shows that during the period of exposure the left heart had no particular load to carry. The work of the right heart increased while the animals stayed at a "high altitude" particularly after the 240th minute; at the same time the pressure in the pulmonary artery and the total pulmonary arterial resistance rose sharply. The increase in the load on the right ventricle was due not only to constriction of the pulmonary vessels, but also to the considerable congestive phenomena in the lungs. Evidence in support of this view is given by determination of the central blood volume and velocity of the blood flow. The time taken for blood to travel from the right heart to the ear at the end of exposure was 180 times its initial value, and the central volume was twice its initial value. Small fluctuations in acid–base balance observed during the first few hours later showed a tendency to decrease, and by the end of exposure the pH of both arterial and venous blood was acid in character, with both gaseous and metabolic components (7.32± and 7.25± respectively). The shift of the blood pH to the acid side was evidently responsible for the decrease in the total resistance of the peripheral vessels. Simultaneously with an increase in the central blood volume, reflecting an increase in filling of the lungs with blood, there was a gradual slowing of the blood flow in the pulmonary system. Although these shifts improved the oxygen saturation of the arterial blood when the partial pressure of oxygen in the alveolar air was low, they also caused an outflow of the liquid part of the blood into the lung tissue. Slowing of the blood flow and stasis in the pulmonary circulation were explained not by weakening of the contractility of the corresponding part of the heart, for phase analysis of cardiac activity revealed that its function was adequate. Most probably these changes were connected with a disturbance of the drainage of blood along the pulmonary veins because of their constriction. This mechanism evidently operates in alveolar hypoxia. The role of increased impulsation from the vascular chemoreceptors can also be assumed, as a result of their excitation by the blood incompletely saturated with oxygen, although such a reaction of the pulmonary vessels is not characteristic of the normal state, it can be postulated that it develops during severe hypoxemia and a disturbance of the diffusion power of the alveolo-capillary membrane. Despite the pH shift to the acid side, no compensatory reaction in the form of hyperventilation was observed. This may be because of lowering of the threshold of excitability of the inspiratory neurons of the respiratory center. Nearly all the animals whose blood oxygen saturation fell below 45-40% developed pulmonary edema. Of course it is no use asserting categorically that a fall in the blood oxygen saturation is the main factor provoking AHAPE. However, comparison of the hemodynamics and gas exchange in animals with and without AHAPE shows that even if the shifts in the respiratory minute volume and the cardiac output are equal, the blood oxygen saturation remains much lower in the first of these conditions, and this confirms that the most probable cause of the lowering of the diffusion power of the lungs was thickening of the alveolo-capillary membrane, with the exclusion of an ever-increasing number of alveoli from the act of respiration because of the effusion of fluid.

The increase in the blood volume in the lungs in turn increases the central blood volume and pressure in the pulmonary vessels even more, and so accelerates the outflow of the

liquid part of the blood into the surrounding tissue. A vicious circle is thus formed. Other no less important factors increasing the outflow of fluid into the lung tissue must also be taken into account. Besides the severe hypoxemia and the increase in the liberation of catecholamines, which are edema-inducing factors, the outflow of sodium ions and their accumulation in the lung tissues, increasing their hydrophobicity, may also play an important role. With an increase in the intensity of pulmonary edema, the ventilation–perfusion ratio is disturbed even more (0.05 compared with 0.71 in the initial state), and in conjunction with the other factors listed above this probably also led to the development of hypoxic edema of the lungs.

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DYNAMICS OF BILE SECRETION IN RATS AFTER SIALADENECTOMY

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KEY WORDS: salivary glands; bile secretion; sialadenectomy.

The role of the external and internal secretory activity of the salivary glands extends far beyond digestion [1-3, 5, 11]. It has been shown that sialadenectomy, loss of the saliva, and obstruction to the salivary ducts are all followed by functional and tissue-structural disturbances in the organs of the gastrointestinal tract, including the hepatobiliary system, and in the biochemical composition of the bile in dogs [6-8].

For these reasons it is interesting to study the relations between function of the salivary glands and liver in animals of other species, notably rats, the bile-secreting apparatus of which has certain morphological and functional peculiarities, and the investigation described below was carried out with that aim.

EXPERIMENTAL METHODS

Experiments were carried out on 150 albino rats weighing 200-250 g, kept on a standard diet with water *ad lib*. There were three series of experiments: I) removal of the sub-

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