

# Influence of High-Altitude Hypoxia on the Hemodynamics of the Small Circle of Blood Circulation and Indicators of Red Blood of Rats

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## ABSTRACT

Studies of the reaction of the small circle of blood circulation and blood condition in response to a long (2, 5, and 10 months) stay of rats at 3200 meters altitude above the sea level (Tien Shan, Tuya-Ashu Pass) have been carried out. It has been established that systolic pressure in the pulmonary artery had increased to 60% by the 2-month period and it has increased throughout the stay in the mountains, with unchanged diastolic. As a result, pulse pressure has increased, which indicates the increase in pulmonary vascular stiffness in the pulmonary artery pool as the main reason for the increase in systolic pressure. The impedance in the lung tissue has significantly increased by 30%, which indicates the restructuring of the blood vessels of the lungs as an expression of the kind of "autoregulation" described for vessels of a large circle

of blood circulation. Blood counts indicate long-term mechanisms of adaptation to high mountains, an increase in the hemoglobin content in red blood cells.

**Keywords:** Transbronchial electrop lethysmography; catheterization; pulmonary hypertension; red blood; high-altitude hypoxia

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## INTRODUCTION

Numerous studies have found that high-altitude hypoxia leads to pulmonary hypertension and stimulation of hematopoiesis [6, 8,12,13]. Moreover, the reaction to the relatively short-term stay of flat animals in the mountains has most often be studied.

However, it is known that aboriginal animals of the highlands and people permanently living in the mountains have significant differences in a number of important indicators of blood and blood circulation (erythrocytosis, increased hemoglobin in red blood cells, redistribution of blood flow in the lungs) [1, 16, 18]. Based on the foregoing and some experimental facts indicating the development of altitudinal deterioration [6, 14], we can assume that even after a long period in the mountains, the adaptation process cannot be regarded as stabilized at a certain level [11,13,19]. In connection with the stated purpose of this work, we have studied the reaction of the pulmonary circulation and blood condition in response to the long-term (2, 5, and 10 months) stay of rats at 3200 meters altitude above sea level (Tien Shan, Tuya-Ashu Pass).

## RESEARCH METHODOLOGY

The experiments were carried out in the summer period on adult Wistar rats, previously (2, 5, and 10 months before the start of the experiment) brought to the base and kept at

room temperature on a normal diet without restriction of water and food. Some animals died during the exposure, and 25 (2 months), 18 (5 months) and 10 (10 months) rats were tested in the experiment. The experiments were performed with natural respiration under nembutal anesthesia (30 mg / kg intraperitoneally) in the position of rats lying on their backs. The hematocrit and hemoglobin content were determined by conventional methods, the number of red blood cells was determined using Picoscale R-4 (Hungary). Pulmonary artery pressure, blood flow in 5 conditionally selected sections of the lungs (apical, ventromedial, ventrobasal, dorsomedial and dorsobasal) were determined by catheterization of the pulmonary artery through the right jugular vein and transbronchial regional electroplethysmography, which allow determining blood flow, blood filling and air content per unit lungs [10,11]. Graphic recording of pressure, electroplethysmogram and electrocardiogram was performed on a jet recorder "Mingoraf-34" (Siemens-Elema), (Fig. 1). The position of the probes of the electroplethysmography in the indicated areas of the lungs was monitored by X-ray diffraction ("Arman-1") in two projections and after opening the animals (Fig. 2). The electrical resistance of the blood taken during the study was determined in a special cuvette (0.2 ml) using the same electroplethysmograph. 35 Wistar rats were tested on the plain to show the results.

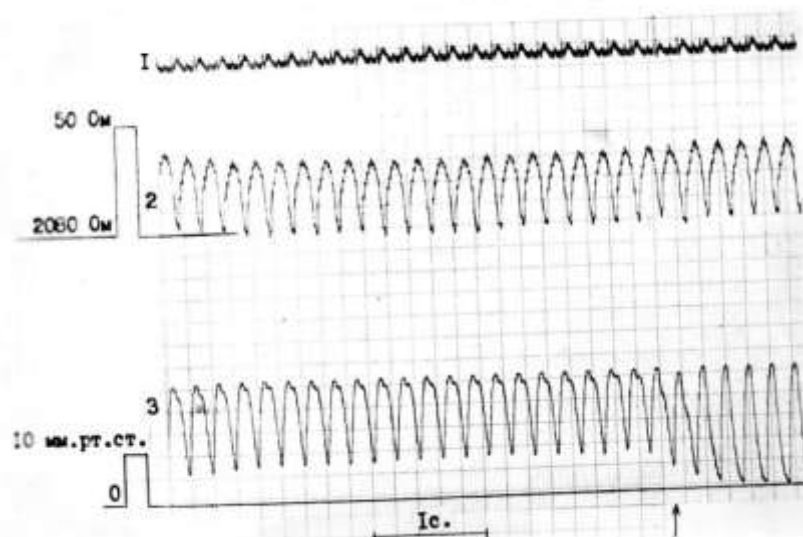


Figure 1. Recording of the electrocardiogram tracings, electroplethysmogram and pressure in the pulmonary artery. Electrocardiogram - 1, electroplate imaging - 2, pressure in the pulmonary artery - 3.

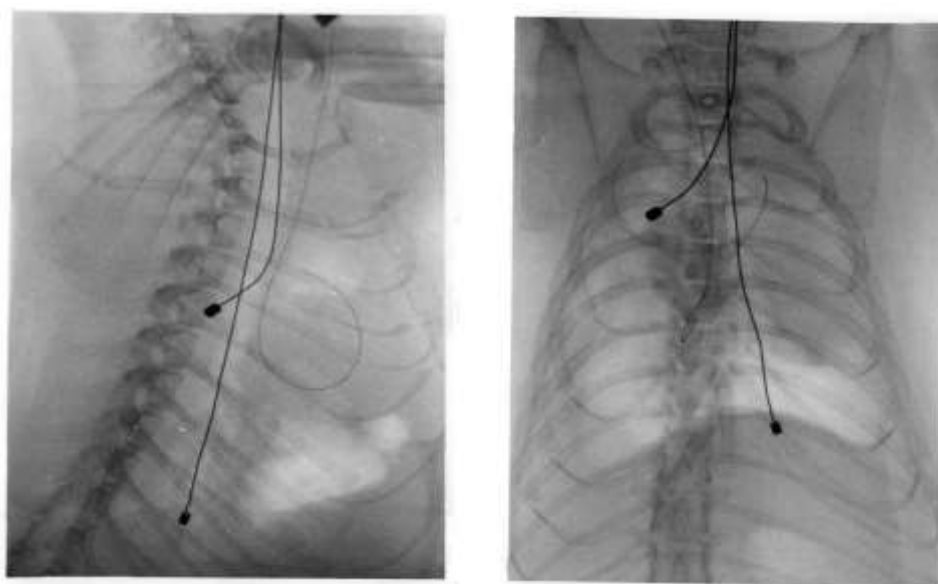


Figure 2. Radiograph of rat chest

a - side view; b - anteroposterior projection. Two electroplethysmograph probes with electrodes at the ends are visible against the background of the pulmonary field. X-ray contrast mandrin placed in the lumen of the catheter, is visible on the contour of the heart at the end of which the lumen of the pulmonary artery is.

The material has been processed statistically using Student's criterion. The result was considered reliable at  $p < 0.05$ .

## RESULTS AND DISCUSSION

It is noteworthy that the mass of animals after 2 months

exposure was 29% lower than in the control, and sold stings decreased steadily (see table). This picture is also observed with a long stay of a person in the mountains [3,9] and is indirect evidence of the lack of stabilization of the adaptation process even for such a long stay for rats in high mountains.

The number of red blood cells at this time, as well as the hematocrit and the electrical resistance of the blood, which mainly depends on the number of red blood cells, did not significantly change compared to the control in that blood) was significantly higher (see table).

Table 1. Pulmonary pressure, red blood index, and rat body weight at different times in the mountains ( $M \pm m$ )

Index	Monitoring	Period of stay in the mountains, months		
		2	5	10
Pressure, inch Hg systolic	22,6±1,0	36,1±2,7**	35,9±3,7**	45,5±4,8**
	12,3±0,8	11,9±1,5	12,6±1,5	12,0±1,9

diastolic				
Electrical resistivity of blood	173±4	172±4	155±6*	174±14
OM·cm	44,2±0,7	45,5±0,6	45,0±2,2	45,4±2,1
Hemoglobin, g / l				
Hematocrit, %	7,42±0,36	6,79±0,31	6,08±0,40*	7,46±0,43
Number of red blood cells, * 10 <sup>12</sup> /l	355±12	254±6**	210±6**	189±16**
Body weight, g				

Note. One asterisk -  $p < 0.05$ , [two -  $p <$  compared to the control.

The systolic pressure in the pulmonary artery by the 2-month period was increased by 60% with unchanged diastolic (see table). As a result, the pulse pressure significantly increased, which indirectly indicated the increase in the stiffness of the vessels of the pulmonary artery basin as the main reason for the increase in systolic pressure. This is confirmed by an approximate calculation of the characteristic impedance [2,4], which reflects the measure of counteraction of rather large vessels of the pulmonary bed to a pulsating blood flow. The impedance has increased approximately by 30%, which may indicate an approximate restructuring of these vessels as an expression of the peculiar "autoregulation" described earlier [5,7] for vessels of a large circle of blood circulation. It should be noted that hypoxic stimulation of carotid and aortic chemoreceptors has also led to a decrease in the extensibility of the pulmonary arteries [4]. As you know, pulmonary hypertension is attributed to the role of redistributive (for blood flow), a functionally

appropriate acting factor [17]. When analyzing the behavior of blood flow and blood supply to the lungs after a 2-month adaptation of rats to high-altitude hypoxia, only in the ventromedial region a significant decrease in these indicators was noted (Pictures. 1 and 2).

Stay in the mountains for 5 months leads to the return of blood flow and blood supply in the mentioned area to the initial level, and increased pressure in the pulmonary artery persists (see the table). The greatest changes in this period are observed in the blood - the electrical resistivity, hematocrit, and the number of red blood cells decrease, but the hemoglobin content continues to increase. This leads to the increase in the oxygen capacity of the blood to 29 ml / 100 ml, which even with a slightly reduced number of red blood cells improves the supply of oxygen to the body. The metabolic shifts, leading to a change in the affinity of oxygen for hemoglobin and an increase in its return to tissues, probably also contribute to this [4].

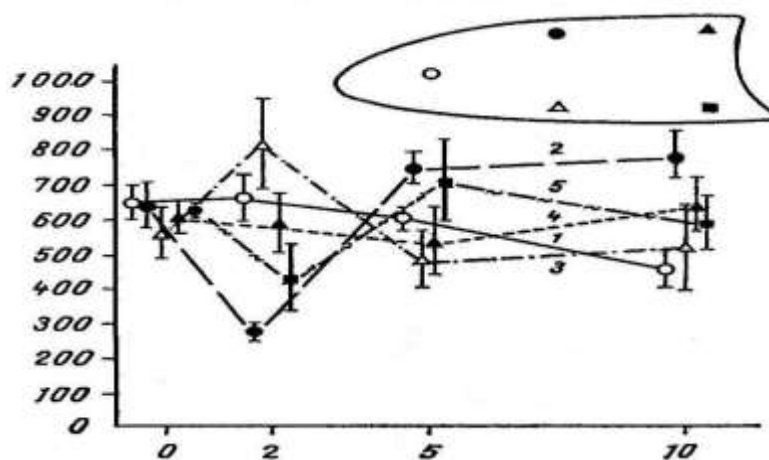


Figure 3. Minute volume of blood flow in the lungs

The ordinate axis is ml / min / 100 cm<sup>3</sup> of lung volume. The abscissa shows months of adaptation. 1 - the apical part of the lung, 2 - ventromedial, 3 - dorsomedial, 4 - ventrobasal, 5 - dorsobasal.

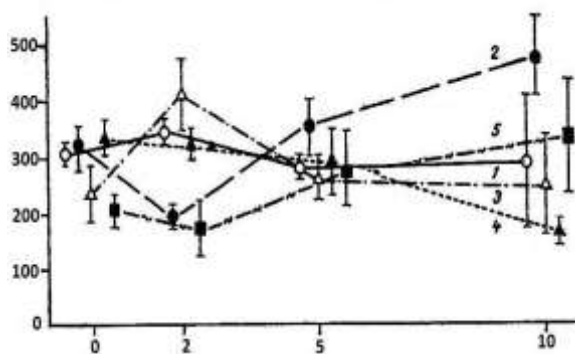


Figure 4. Average blood supply

On the ordinate axis - ml / 100cm<sup>3</sup> of lung volume of various lung sections in rats at different periods of stay in the mountains. The remaining notation is the same as in fig. 1.

At the 10-month adaptation stage (Picture 3), a further increase in systolic pressure is observed in the absence of an increase in diastolic pressure (see table). Blood flow increases in the ventromedial region, while in the apical region, while in the apical part of the lung, it significantly

decreases (see Picture 1). According to the severity of the blood supply reaction, the ventromedial region is again the most labile (see Picture 2). The mechanisms of this redistribution are still unclear and do not fit into the well-known schemes of a more uniform regional blood flow in conditions of high-altitude hypoxia [12, 13]. Probably, in this case, more complex adaptive rearrangements of the cardiovascular system occur [2.5].

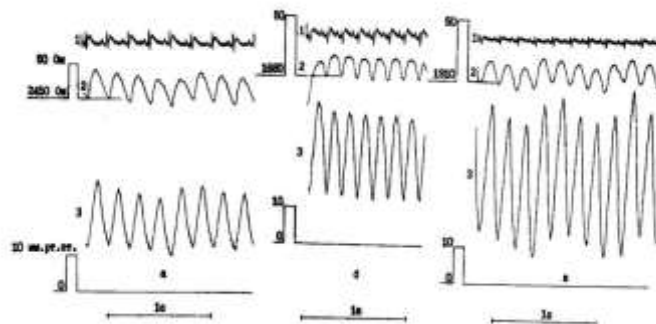


Figure 5. Pressure curves in the pulmonary artery and electroplethysmogram of rats at different periods of stay in the mountains: a - 3 days, b - 60 days, c - 300 days

1- Electrocardiogram, 2- electroplethysmogram of the dorsal base of the lung, 3- pressure in the pulmonary artery; The calibration signals and the basic value of the electrical resistance, as well as zero pressure, are shown at the left of the curves. At the bottom is the time stamp.

## CONCLUSION

The tests and proved facts show that one of the constantly and long-acting mechanisms of adaptation to high altitude is an increase in the hemoglobin content in red blood cells and a corresponding increase in the oxygen capacity of the blood. Along with a change in the hemoglobin dissociation constant and adaptation to hypoxia at the tissue level [1, 7], this forms the basis of an energetically more favorable adaptive mechanism. The role of red blood cells in the conditions of the Tien Shan high mountains, apparently, is not so significant, at least at earlier dates in the mountains [6, 8].

As for the role of pulmonary hypertension, as our study has shown, systolic type hypertension, additional studies are needed here to clarify both the intimate mechanisms of its origin and its role in the regional redistribution of blood flow and blood supply to the lungs.

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