EFFECT OF THE TOXIN OF *Pasteurella pestis* ON THE RESPIRATORY FUNCTION OF THE BLOOD AND ON CERTAIN HEMODYNAMIC INDICES

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The study of the respiratory function of albino rats with Pasteurella pestis toxemia began with investigation of the principal indices of external respiration: the character and number of the respiratory movements, the pulmonary ventilation, the oxygen consumption, and the carbon dioxide elimination [2]. Analysis of the results of these investigations showed that the oxygen lack developing in the course of P. pestis toxemia is the result, not only of a disturbance of external respiration, but also of a disturbance of the blood and circulatory systems or of injury to the respiratory center by the toxin.

The object of the present investigation was to study the hemodynamic indices in albino rats following injection of P. pestis toxin into these animals.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats weighing 160-180 g. The toxin used consisted of fraction II obtained by Baker's method from P. pestis strain EB 229. All the investigations were made 4 h after intraperitoneal injection of 3 LD_{50} of P. pestis toxin. Altogether 167 animals were used in the investigation.

The circulating blood volume was determined by the method of dilution of dye in the plasma. The dye used was a 1% solution of Congo red. The plasma for testing and the standard solution were examined colorimetrically in a type FEK-M photoelectric colorimeter with a green filter.

To the volume of circulating plasma thus obtained was added the volume of the blood cells, determined by

TABLE 1. Effect of P. pestis Toxin on Hemodynamic Indices and Red Blood Picture in Albino Rats

Group of rats	No. of animals	Vol. of circulating plasma (in ml)	Vol. of circulating erythrocytes (in ml)	Circulating blood vol. (in ml)	Blood system	
					hematocrit index	erythrocyte count
Control	10	6,5±0,42	4,7±0,36	11,2±0,81	42±0,66	7 170 000 ±115 000
Experimental (investigated 4 h after injection of 3 LD_{50} toxin)	10	3,9±0,08	4,2±0,32	8,1±0,58	51±1,20	8 820 000± ±290 000
Change in indices studied (in %)		60,0	89,3	72,3	121,4	125,7

TABLE 2. Effect of P. pestis Toxin on Gaseous Composition of Arterial and Venous Blood of Albino Rats

Group of rats	Number of animals	Arterial blood (in vols. %)		Venous blood (in vols. %)		Arteriovenous difference		Percentage of utilization of oxygen	Coefficient of unsaturation of capillary blood
		carbon dioxide	oxygen	carbon dioxide	oxygen	carbon dioxide	oxygen		
Control	24	41.1± 0.66	19.2± 0.29	50.4± 0.88	14.2± 0.30	4.9± 0.06	9.0± 0.60	25.2± 0.66	3.2± 0.10
Experimental (investigated 4 h after injection of 3 LD_{50} of toxin)	11	37.5± 0.90	18.2± 0.31	46.2± 1.21	10.5± 0.35	7.7± 0.29	8.9± 1.10	42.0± 1.50	5.7± 0.30

means of the hematocrit. At the same time the erythrocyte count was determined by the usual method, using a Goryaev's chamber.

The gaseous composition of the blood was investigated in a Van Slyke's manometric apparatus. The alkaline reserve of the blood was determined by a volumetric method in a Van Slyke's apparatus. For estimation of the hemodynamic indices in normal conditions blood was taken from some animals (controls), and for investigation of these same indices after injection of the toxin, blood was taken from other (experimental) animals. The experiments were acute in character, and after withdrawal of blood for investigation, all the animals were sacrificed.

The mean data of a series of parallel determinations (M), the mean error (m), and the number of observations (n) are given in the tables.

EXPERIMENTAL RESULTS

It is clear from Table 1 that after injection of P. pestis toxin the circulating blood volume fell by 27.7%, the plasma volume by 40%, and the volume of the erythrocytes by only 10.7%. Consequently, the decrease in the circulating blood volume in the experimental animals took place mainly on account of a decrease in the volume of plasma.

These results suggest that in P. pestis toxemia disturbances of the permeability of the vascular wall and escape of plasma into the tissues take place, causing hemoconcentration. Changes observed in the blood system—an increase in the number of erythrocytes/mm^3 blood and in the hematocrit index confirmed the existence of hemoconcentration. The disparity between the reduction of the plasma volume and the reduction of the circulating blood volume suggested that in addition to the changes in vascular permeability and to the escape of plasma into the tissue interspaces, some blood is retained in depots in the internal organs.

The problem of the possible formation of blood depots was investigated by determining the weight of the organs every hour after injection of the toxin. It was assumed that if blood was retained in a particular organ, its weight would be bound to increase. The lungs, spleen and liver from animals of identical weight were examined in this manner. The results of this series of experiments demonstrated a significant increase in the weight of the spleen and a tendency for the weight of the liver and lungs to increase. The average general increase in weight of the organs so investigated was 4%. Hence, the decrease in the circulating blood volume in albino rats with P. pestis toxemia results mainly from escape of plasma from the blood stream and from the retention of small volumes of blood in depots in the internal organs.

Four hours after injection of the P. pestis toxin, the oxygen concentration in the venous blood fell by 3.7 vols. %, the arteriovenous difference rose to 7.7 vols. %, and the percentage utilization of oxygen by the tissues was 42 (Table 2). These well defined changes in the gaseous composition of the blood of the investigated rats are characteristic of the circulatory type of hypoxia, of which they are the principal signs. Additional evidence of the development of circulatory hypoxia was given by the changes in the hemodynamic indices in the experimental animals.

Besides the signs of circulatory hypoxia noted above (Table 2), elements of other types of hypoxia were also present in the gaseous composition of the blood of the investigated animals. For example, the reduction in the oxygen concentration in the arterial blood 4 h after injection of the toxin demonstrated the presence of developing hypoxic hypoxia.

At first glance the fall in the oxygen concentration in the arterial blood appears insignificant. Taking account of the hemoconcentration (see Table 1), however, it is evident that the percentage unsaturation of the arterial blood of the investigated animals with oxygen was not 13.4%, as shown in Table 2, but 26.7%. Consequently, the hypoxic hypoxia developing in the pathological state caused by injection of P. pestis toxin is considerable in degree.

During further analysis of the changes in the gaseous composition of the blood of the animals poisened with the toxin, attention was directed to the increase in the utilization of oxygen from the arterial blood by 16.8% and the accompanying decrease in the carbon dioxide concentration in the venous blood by 4.2 vols. %. The latter may be associated with a disturbance of the tissue metabolism in the process of P. pestis toxemia and with the appearance of products of incomplete oxidation.

If this suggestion is true, the appearance of incompletely oxidized products of metabolism in the blood must give rise to a change in the acid-base balance of the blood of the investigated animals, with an accumulation of acids in the organism and a corresponding decrease in the alkaline reserve of the blood.

To test this hypothesis a series of experiments was carried out to determine the alkaline reserve of the blood of 33 control animals and 14 experimental animals 4 h after injection of 3 LD_{50} of P. pestis toxin. In the former it was 45.1 ± 0.56 and in the latter 26.6± 0.83. The decrease in the alkaline reserve of the blood of the investigated animals was evidence of developing acidosis of nongaseous type and of a considerable disturbance of the tissue metabolism.

Hence, albino rats with P. pestis toxemia develop considerable oxygen lack. In this condition, as in the case of plague infection [3], the picture of hypoxia exhibits elements of three types of oxygen lack (in our observations, circulatory, hypoxic, and histotoxic hypoxia).

It seems that the principal role in the development of the hypoxic state belongs to the hemodynamic disorders expressed by a reduction of the circulating blood volume, by hemoconcentration, and by a slowing of the rate of blood flow. In turn, the presence of circulatory hypoxia may lead to the development of other types of hypoxia [1, 4, 6].

However, direct changes in the biological properties of hemoglobin as an oxygen carrier [3] in P. pestis toxemia cannot be excluded, and these may be the cause of the hypoxic hypoxia. On the other hand, the cause of the development of histotoxic hypoxia may be the direct action of P. pestis toxin on the tissue respiratory enzymes [7]. Further investigations of this problem will be undertaken.

SUMMARY

A study of the hemodynamic indices and blood picture during plague intoxication has demonstrated that intraperitoneal injection of P. pestis toxin into albino rats causes hemoconcentration and reduces the circulating blood volume chiefly at the expense of plasma discharge into the interstitial spaces.

Oxygen deficiency developing during plague intoxication includes elements of circulatory, hypoxic and histotoxic hypoxia, the leading role being played by the circulatory type of hypoxia.

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