is relatively stable, and no signs of anemia described by some authors [8, 14] could be observed in old mice. These findings agree with the results reported by other authors who, too, found basal erythropoiesis to be unchanged in old mice [10, 12].

Old mice, on the other hand, showed impaired humoral regulation of erythropoiesis, manifested in elevated serum erythropoietic activity as compared to young animals. Such high activity is characteristic for neonatal mice [9] in which, however, it is associated with the anemia that accompanies the rapid growth of tissues and is a reflection of their deficient oxygen supply. In contrast, the high erythropoietic activity in the sera of old mice could not be due to the impact on erythropoiesis of factors other than erythropoietin given that this activity, when measured in the murine serum by the in vitro bioassay we used, depends almost entirely on the presence of erythropoietin rather than on growth factors [11].

In old mice, the altered ratios of formed elements and plasma in the blood [8], the accelerated proliferation of erythroid cells, and the elevated activities of certain enzymes involved in erythropoiesis [10] may be consequences of possible disorders in bone marrow functions. In addition, the existing evidence regarding abnormalities in the cellular composition and functional activity of the hematopoietic microenvironment in old mice [13] suggests that the mechanisms whereby bone marrow cells and the hematopoietic microenvironment interact undergo changes with advancing age.

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Enterosorption Normalizes the Level of Biogenic Amines in Experimental Bronchospasm

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Recent studies have demonstrated beneficial effects of enterosorption on the clinical course of bronchial asthma. Sorbents of the new generation (Polyphepan, OKN-P, AUVM-Dnepr-MN, and others) administered *per os* have been found to enhance the efficacy of drug treatment in cases of exacerbated asthma and to accelerate the onset of remission [2, 3, 5, 10].

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TABLE 1. Respiratory Parameters at Various Times in the Course of Bronchospasm in the Control, Test, and Intact Groups of Rats (Means ± SD)

Parameter	Intact rats	Baseline values		30 min after challenge	
		Control rats	Test rats	Control rats	Test rats
Breathing frequency, min	84.72±4.23	82.88±4.49	87.85±4.11	54.39±6.51	73.57±4.63*
Duration of inspiration, sec	0.36±0.04	0.38±0.02	0.36±0.02	0.43±0.04	0.38±0.04
% of normal value	-	100	100	113	106
Duration of expiration, sec % of normal value	0.41±0.03	0.42±0.02	0.43±0.02	1.09±0.10*	0.48±0.04*
% of normal value	-	100	100	260	112
Duration of inspiration/duration of expiration	0.87±0.04	0.91±0.08	0.84±0.09	0.39±0.05*	0.79±0.03*
% of normal value	-	100	100	43	94
Severity of dyspnea, units	0	0	0	1.16	0

Note. The asterisk denotes a significant difference between the test and control groups at $p<0.05$.

A critical role in the pathogenesis of asthma is known to be played by histamine, serotonin, and some other neurotransmitters of bronchospasm [11-13, 15]. When the producer cells are degranulated, histamine and serotonin are released from them very rapidly and can increase the tone of bronchial smooth muscles, suggesting that these bioamines are among the major neurotransmitters responsible for the clinical manifestations of asthma [15]. So far, animal models of bronchospasm have been used to reproduce only one component of asthma pathogenesis, namely the one involving the production of reactive antibodies and the release of neurotransmitters. Animal models, however, can also help in identifying the major mechanisms of bronchospastic processes and provide a basis for the development of novel approaches to the treatment of asthma [6].

The main objective of the present study was to assess the efficacy of enterosorption in animals with experimentally induced bronchospasm by determining how an enterosorbent affects the concentrations of biogenic amines such as histamine (HI) and serotonin (ST) in the blood and organs of the test animals.

MATERIAL AND METHODS

The experiments were carried out on 300 rats weighing 150-200 g. Bronchospasm was produced through sensitization of the test rats with egg albumin for a period of two weeks, followed by intravenous administration of a challenging dose of the albumin (1 mg/kg body weight). For the sensitization, an egg albumin solution was injected intraperitoneally on two occasions in a dose of 1 mg/kg together with an adjuvant (aluminum hydroxide gel). The rats were divided into three groups intact (nonsensitized), test, and control. The test rats received an enterosorbent (Polyphepan) at 1 g/kg daily throughout the two-week period of sensitization, while the control rats were left untreated. The magnitude of respiratory abnormalities was evaluated by noting changes in the frequency, amplitude, and form of respiratory movements registered using a specially designed sensor. HI and ST levels in the blood and in lung, liver, and gut homogenates were measured by fluorimetry [14]. In an additional experiment, the tissue distribution of these biogenic amines and their transport from the tissues to the intestinal lumen were examined after

TABLE 2. Histamine and Serotonin Levels (μg/ml) in the Blood and Organs of the Control, Test, and Intact Groups of Rats (Means ± SD)

Organ/blood	Intact rats		Control rats		Test rats	
	Histamine	Serotonin	Histamine	Serotonin	Histamine	Serotonin
Lung, %	2,4±0,14	1,44±0,07	5.7±0,3*	2,98±0,15*	2,2±0,12**	2,24±0,05**
	100	100	237,5	206,9	93,3	72,2
Blood, %	0,09±0,005	0,072±0,005	0,16±0,007*	0,18±0,006*	0,07±0,002**	0,08±0,002**
	100	100	177,8	250	77,8	114,3
Liver, %	1,17±0,04	1,02±0,08	2,11±0,07*	2,19±0,09*	0,99±0,06**	0,95±0,03**
	100	100	180,3	214,7	84,6	93,1
Intestine, %	5,6±0,11	3,35±0,2	8,5±0,12*	4,95±0,2**	3,39±0,11**	2,81±0,09**
	100	100	151,8	147,8	60,5	83,9

Note: * $p<0.05$ relative to intact rats; ** $p<0.05$ between control and test rats.

injecting nonsensitized rats intraperitoneally with tritium-labeled HI and ST in a dose 3×10^5 cpm; activities of the labeled amines were measured in a β counter [1].

RESULTS

Analysis of the respiratory parameters in rats of the control group showed that bronchial obstruction after challenge with the allergen developed gradually and was most pronounced after 30 min. At that time, the presence of bronchospasm was reflected in bradypnea and a 57% reduction, on average, in the ratio between the durations of inspiration and expiration (Table 1). In the test rats administered the enterosorbent, the bronchospasm was much less severe or did not develop at all.

The control rats also showed elevated HI and ST levels in the blood and in the three organs where they were measured (Table 2), which may be attributed both to enhanced synthesis of these neurotransmitters of bronchospasm during the sensitization [8] and to their impaired metabolism as a result of inhibited monoamine oxidase activity [4]. It has been shown that the immunological "conflict" arising after allergen administration causes HI and ST to be released from enterochromaffin cells, mast cells, platelets, and basophils, with a rapid rise of these neurotransmitters in the lungs and liver, which play dominant roles in their inactivation [6]. Our findings confirmed this. Thus, HI levels in the lungs, liver, and blood of control rats exceeded by 138%, 80%, and 78%, respectively, those found in the intact animals. Similar differences between the two groups were observed for ST.

In the enterosorbent-treated group HI and ST levels were the same or, in most rats, even lower than in the intact group. In the intestine, for instance, the mean HI concentration in the test group was 39% lower and the ST concentration 16% lower.

In the experiment where the tissue distribution of HI and ST and their transport from the tissues to the intestine were studied on nonsensitized rats, the total amount of labeled HI and ST in the Polyphepan-treated animals was significantly (1.5-fold) lower than in the untreated animals. As early as 10 min postadministration, 2% to 4% of the total administered activity was found to have been adsorbed on the Polyphepan, indicating that the biogenic amines, in diffusing into the intestine within plasma components, came into contact with, and were partially fixed on, the sorbent's surface. Further evidence that enterosorbents can block absorption of biogenic amines at the level of the intestinal histohematic barrier was provided by the finding that the livers of Polyphepan-treated rats contained, on average, 60% less HI that did those of untreated controls. Our results suggest that enterosorbents such as Polyphepan can bind HI and ST at the intraintestinal level of their hepatoenteral and hemoenteral cycles, with a concurrent enhancement, in an indirect way, of the mechanisms through which the concentrations of these neurotransmitters of bronchospasm are lowered in the blood and various tissues.

In conclusion, one mechanism whereby enterosorption exerts its therapeutic effects in bronchospastic conditions appears to be reductions in the concentrations of bioamines in biological fluids and tissues through enhancement of their intestinal transport and absorption.

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