thyroid extract. Between three and four days after administration of thyroid to the animals the period of increased acid formation occurs in the stomach, and is followed by a period of inhibition of the intensity of acid formation in response to a food stimulus.

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EFFECT OF NEUROMEDIATORS ON THE ACID–BASE BALANCE

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Acute and chronic experiments on dogs showed correlation between the state of the adrenergic, cholinergic, and serotoninergic systems, on the one hand, and the acid–base balance of the animal on the other hand. An excess of each mediator was accompanied by respiratory alkalosis and a deficiency by mixed respiratory and metabolic acidosis.

KEY WORDS: *acid–base balance; catecholamines; acetylcholine; serotonin.*

Neuromediators are known to play an important role in the regulation of the hemodynamics in general and the nutritive circulation in particular [2, 13, 15]. The role of mediator systems in the regulation of the acid–base balance is particularly interesting. However, information on this problem is extremely limited [3].

The object of the investigation described below was, accordingly, to study the correlation between the acid–base balance (ABB), as an integral indicator of the state of the nutritive circulation, and the level of the most important neuromediators of the blood.

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TABLE 1. Indices of Functional State of Adrenergic, Cholinergic, and Serotoninergic Systems and Acid–Base Balance in Dogs with Experimentally Produced Excess of the Corresponding Mediator (M ± m)

Index studied	Procedure	Control	Experiment
CCh	Injection of adrenalin and noradrenalin	4,0±0,057	7,8±0,073
pH		7,35±0,003	7,42±0,004
pCO_2		36,64±0,282	28,0±0,482
BE		—4,1±0,124	+2,0±0,960
SB		20,5±2,361	26,0±1,130
ACh	Injection of acetylcholine	3,9±0,134	7,7±0,095
BChE		6,9±0,127	10,0±0,053
AChE		12,4±0,162	17,4±0,169
pH		7,35±0,005	7,42±0,012
pCO_2		36,63±0,395	30,0±1,246
BE		—4,5±0,234	—4,5±0,864*
SB		20,5±2,360	20,5±2,360*
ACh	Injection of lipocaic	3,8±0,095	4,9±0,099
AChE		7,1±0,254	8,7±0,074
BChE		12,7±0,314	14,8±0,131
pH		7,34±0,006	7,45±0,020
pCO_2		38,0±0,389	29,0±0,967
BE		—3,5±0,960	—3,0±0,018
SB		21,5±2,436	21,5±2,436*
5-HT	Injection of tryptophan	0,90±0,036	2,00±0,032
MAO		3,85±0,098	6,34±0,125
pH		7,35±0,003	7,39±0,002
pCO_2		36,64±0,282	31,917±0,484
BE		—4,10±0,095	—3,4±0,018
SB		20,5±2,360	21,0±1,124*
5-HT	Injection of serotonin	0,80±0,038	1,2±0,044
MAO		4,9±0,082	5,7±0,119
pH		7,36±0,004	7,38±0,003
pCO_2		37,66±0,395	32,00±0,360
BE		—3,5±0,124	—4,083±0,354
SB		19,92±0,934	19,72±0,966*

Legend to Tables 1 and 2: 1. CCh) total catecholamines (in µg%); ACh) acetylcholine (in µg/ml; AChE) acetylcholinesterase [in mg/(ml•h)]; BChE) butyrylcholinesterase [in mg/(ml•h)]; 5-HT) serotonin (in µg/ml); MAO) monoamine oxidase activity [in µg/(ml•h)]; pH) negative $\log_{10}$ of hydrogen ion concentration; pCO_2) partial pressure of CO_2 in blood (in mm Hg); BE) buffer base excess of deficiency (in meq/liter); SB) standard bicarbonates (in meq/liter). 2. *Indicates indices whose difference from control is not significant, $P > 0.05$; in all other cases $P < 0.005$.

EXPERIMENTAL METHOD

Experiments were carried out on 78 dogs of both sexes weighing 7-14 kg. All the animals were divided into three main groups. In Group 1, consisting of 24 dogs (4 series of experiments, 6 animals in each series) the role of functional activity of the sympathicoadrenal system in the regulation of ABB was studied. In Group 2, in 30 animals (5 series of experiments, 6 dogs in each series) the dependence of the indices of ABB on activity of the cholinergic system was investigated. In Group 3, in 24 animals (4 series of experiments, 6 dogs in each series) activity of the serotoninergic system was studied and compared with the indices of ABB.

An artificial excess of catecholamines was created by injection of a combination of adrenalin and noradrenalin, 100 µg/kg of each, twice a day for 7 days subcutaneously. A catecholamine deficiency was produced by extirpation of the chromaffin tissue of the adrenals as a result of total removal of the right adrenal and thermocauterization of the medulla of the left adrenal [4], or blockage of α- and β-adrenoreceptors was produced by injection of the α-adrenoblocker droperidol in a dose of 0.1 mg/kg and of the β-adrenoblocker propranolol (obsidan) in a dose of 1 mg/kg daily for 7 days subcutaneously.

TABLE 2. Indices of Functional State of Adrenergic, Cholinergic, and Serotoninergic Systems and Acid–Base Balance in Dogs with Experimentally Induced Deficiency of the Corresponding Mediator (M ± m)

Index studied	Procedure	Control	Experiment
CCh	Demedullation	3,9±0,089	0,11±0,024
pH		7,36±0,002	7,32±0,005
pCO_2		36,25±0,250	42,0±0,570
BE		—3,5±0,960	—5,0±0,124
SB		21,25±2,330	20,5±2,360*
CCh	Injection of droperidol and propranolol	3,8±0,090	0,10±0,010
pH		7,36±0,003	7,30±0,003
pCO_2		36,41±0,280	40,6±0,287
BE		—4,16±0,234	—8,4±0,345
SB		20,833±2,360	21,3±1,124*
ACh	Depancreatization	4,0±0,117	0,6±0,049
AChE		6,1±0,138	3,0±0,117
BChE		12,1±0,183	5,8±0,240
pH		7,36±0,003	7,30±0,003
pCO_2		36,41±0,286	45,0±0,584
BE		—4,16±0,864	—4,0±0,234
SB		20,833±0,819	21,0±1,124*
5-HT	Injection of reserpine	0,996±0,032	0,05±0,044
MAO		3,8±0,386	1,0±0,060
pH		7,36±0,002	7,325±0,004
pCO_2		36,25±0,250	40,66±0,581
BE		—3,5±0,865	—5,5±0,130
SB		21,25±1,124	20,083±1,054*
5-HT	Depancreatization	0,9±0,065	0,07±0,006
MAO		5,1±0,132	2,5±0,206
pH		7,36±0,003	7,33±0,001
pCO_2		36,41±0,280	43,0±0,484
BE		—4,16±0,234	—3,5±0,960
SB		20,833±1,054	21,25±1,124*

In the next series of experiments, performed on adrenalectomized animals receiving adrenalin and noradrenalin each in a dose of 100 μg/kg, the ATP indices and total blood catecholamine concentration were determined.

An artificial excess of cholinergic mediator was produced by intraperitoneal injection of acetylcholine in a dose of 100 μg/kg daily for 7 days or administration of the hormone lipocaic in a dose of 50 units daily for 8 days by mouth.

An experimental deficiency of this mediator was produced by partial depancreatization. Additionally two series of experiments were carried out on the depancreatized dogs, which received acetylcholine in a dose of 100 μg/kg or lipocaic in a dose of 50 units daily after the operation and until the day of the experiment in order to compensate the disturbed process of acetylcholine formation.

To produce an experimental excess of serotonin in the body the method of exogenous administration in a dose of 100 μg/kg body weight or injection of tryptophan in a dose of 100 μg/kg intraperitoneally daily for 10 days was used [5].

A deficiency of the serotoninergic complex was produced by partial depancreatization and also pharmacologically, by the method of reserpine "priming" in a dose of 5 mg/kg daily for 10 days.*

In the next series of experiments the depancreatized animals received an injection of exogenous serotonin in a dose of 100 μg/kg for the purpose of compensation.

The ABB was studied on the AZIV-2 apparatus (USSR) and whole blood was used. The principal indices of ABB, namely pH, pCO_2, BE, and SB, were calculated by the Siggaard-Andersen nomogram [1]. Other parameters determined included the total catecholamine level, by Shaw's method in Matlina's modification [7], the acetylcholine level by Corsten's biological method and by Shutskii's chemical method [10, 12], acetyl- and butyrylcholinesterase activity by Hestrin's chemical method [14], the serotonin level by the biological method of Dalgliesh

*The catecholamine deficiency arising under these circumstances was compensated by injection of adrenalin and noradrenalin in doses of 100 μg/kg before the experiment.

et al. [11] on the albino rat ileum, and monoamine oxidase (MAO) activity by Soloimskaya's method based on the decrease in serotonin [8]. The significance of differences was determined by Student's criterion.

EXPERIMENTAL RESULTS

The experimental results are given in Tables 1 and 2. As Table 1 shows, administration of adrenalin and noradrenalin led to an increase in the total blood catecholamines and was accompanied by a shift of the ABB indices toward respiratory alkalosis. After demedullation the catecholamine content fell and the ABB indices were shifted toward mixed respiratory and metabolic acidosis. The same effect was observed after administration of droperidol and propranolol to block α- and β-adrenoreceptors (Table 2).

An excess of cholinergic mediator created either by injection of acetylcholine into intact animals or by injection of lipocaic, which plays a role in acetylcholine formation, was accompanied by increased blood cholinergic activity and a shift of the ABB indices toward respiratory alkalosis (Table 1).

In experimental acetylcholine deficiency induced by partial depancreatization, on the seventh to eighth day after the operation the activity of the blood cholinergic system was reduced and the ABB indices were shifted toward mixed respiratory and metabolic acidosis (Table 2).

With an excess of serotonin in the peripheral blood, whether produced by injection of serotonin itself or of its precursor (tryptophan), increased activity of the serotoninergic system and a shift of ABB indices toward respiratory alkalosis were observed (Table 1). In serotonin deficiency induced by partial depancreatization, the activity of the blood serotoninergic system on the 12th-16th day after the operation was reduced and the ABB indices were shifted toward respiratory acidosis. In the next series of experiments the animals were given resperpine, a drug which inhibits the biological activity of serotonin. In this group of animals the serotonin concentration and MAO activity in the peripheral blood fell, whereas the ABB indices were shifted toward mixed respiratory and metabolic acidosis (Table 2).

In animals with an experimentally induced deficiency of the corresponding mediator, which was compensated by its injection, the functional state of the adrenergic, cholinergic, and serotoninergic systems was changed only very little, and the ABB indices were within normal limits.

The results are evidence that neuromediators (catecholamines, acetylcholine, and serotonin) influence the ABB. The action of each of these neuromediators on the ABB indices is identical in type. As regards the mechanisms of this effect, it can first be assumed to be produced indirectly through changes in the nutritive circulation, for neuromediators are known to play a role in the regulation of the hemodynamics and of vascular permeability [9]. However, there is also evidence of the trophic action of chemical mediators, i.e., of their direct participation in metabolic processes [6].

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