VARIATIONS IN THE BLOOD BROMINE LEVEL DURING SENSITIZATION, ANAPHYLACTIC SHOCK AND THE POSTSHOCK PERIOD

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The interrelationship of the blood bromine level and the character of the relation between the main nervous processes – excitation and inhibition – in the cerebral cortex was first shown by I. P. Pavlov's collaborators L. M. Georgievskaia, M. K. Petrova and M. A. Usievich [4, 7]. Subsequently it became evident that dogs with different types of nervous systems exhibited definite fluctuations in the blood bromine level, characteristic for the given type [2], that interference of the food and defense reactions caused a sharp disturbance of stability in this level [1] and that radium irradiation of the animal's head was accompanied by a decrease in bromine concentration in the blood [6].

The present work is concerned with the determination of dynamics of the blood bromine level in dogs under normal conditions and in various stages of the anaphylactic state, starting from the moment of protein sensitization and finishing with the postshock period.

EXPERIMENTAL METHODS

Bromine concentration in the blood was determined by Greenberg's micromethod [9], based on van der Meilen's principle and consisting of oxidation of bromides to bromates with subsequent iodometric titration. In carrying out long-term experiments on the dynamics of fluctuation in the blood bromine level it is essential that the experimental animals be maintained on a constant diet, since different foodstuffs have extremely variable bromine content. Moreover, it is essential to take into account the definite interrelations of bromine and chlorine in the organism. Cases have been described in which a sharp rise in blood bromine was noted in patients who had been using a great deal of common salt in their food [10].

The animals were sensitized with normal horse serum according to the generally accepted method. The serum was administered on 3 successive days in doses of 0.2 ml per 1 kg body weight (subcutaneously on 2 days, intravenously on the 3rd day). Anaphylactic shock was produced on the 20th-23rd day from the moment of sensitization by means of a booster dose of specific serum (2 ml per 1 kg body weight).

EXPERIMENTAL RESULTS

Table 1 shows the data of 11 experiments, giving the extreme fluctuations in the blood bromine level before and during sensitization. In most dogs the fluctuations in the blood bromine content were within the limits of 0.1 mg%, but in isolated cases these fluctuations amounted to 0.15-0.26 mg%. Such variability among dogs with respect to blood bromine content had been noted previously (M. F. Vasil'ev [2]).

During sensitization, beginning with the 8th day after administration of the first sensitizing dose, the majority of cases showed a tendency to decrease blood bromine concentration. In one dog (protocol 5) an increase of blood bromine level from 1.292 to 1.596 mg% was observed during the period of sensitization. The extreme fluctuations in the blood bromine level observed during the different days of sensitization exceeded considerably those limits which were characteristic for the dogs prior to sensitization. This was particularly pronounced at the height of anaphylactic state, i.e., during the days of the most violent reaction to repeated injection of the antigen. It is

TABLE 1

Extreme Fluctuations of Blood Bromine Levels in Dogs in the Normal State and During Sensitization

No. of experiment	Fluctuations of bromine levels in the normal (in mg %)	Fluctuations of blood bromine levels on successive days of sensitization (in mg %)					
		1–4	5–7	8–12	13–16	17–19	20–23
1	0.813	0.912	0.760	0.988	0.646	0.342	0.372
	0.912	0.912	0.836	1.140	0.684	0.380	0.752
2	1.064	1.064	0.676	0.646	0.646	0.364	0.121
	1.140	1.064	0.684	0.760	0.691	0.524	0.380
3	0.676	0.304	0.433	—	—	0.281	0.235
	0.760	0.380	0.433	—	—	0.357	0.934
4	0.889	0.912	0.380	—	—	0.836	0.630
	0.988	0.919	0.836	—	—	0.912	0.874
5	1.064	1.140	0.836	1.444	0.988	0.912	0.836
	1.140	1.292	1.444	1.520	0.988	1.596	1.064
6	0.912	0.836	0.737	—	—	0.380	0.380
	1.064	0.836	0.737	—	—	0.532	0.942
7	0.304	0.228	0.205	0.152	0.190	0.190	0.152
	0.326	0.456	0.205	0.319	0.205	0.448	0.471
8	0.532	0.532	0.380	0.228	0.167	0.144	0.136
	0.653	0.585	0.380	0.304	0.190	1.144	0.448
9	0.372	0.372	0.167	0.167	0.205	0.152	0.722
	0.418	0.380	0.304	0.228	0.304	0.212	0.828
10	0.190	0.197	0.152	0.114	0.076	0.091	0.091
	0.342	0.212	0.190	0.152	0.136	0.121	0.152
11	0.471	0.478	0.311	0.273	0.250	0 205	1.197
	0.737	0.684	0.494	0.357	0.305	0.372	0.668

TABLE 2

Fluctuations of Blood Bromine Level in Dogs During Anaphylactic Shock

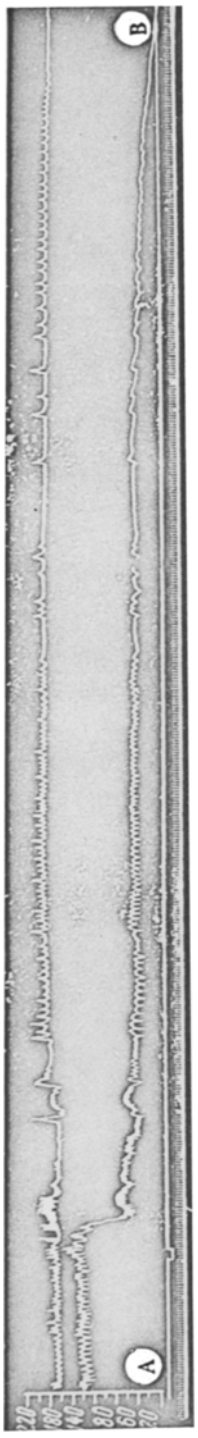
No. of experiment	Initial blood bromine level (in mg %)	Time in minutes from the booster administration of serum and the corresponding blood bromine levels (in mg %)						Outcome of shock
		2–5	10–15	20	30	40–50	60–180	
1	0.76	3.42	3.42	5.32	--	2.40	0.13	Alive
2	0.38	3.31	4.25	3.72	0.11	—	—	Died
3	0.93	0.53	0.47	0.22	—	—	—	"
4	0.63	3.61	3.30	3.34	—	2.88	3.26	Alive
5	0.83	2.88	1.59	—	2.28	2.35	2.50	"
6	0.88	2.58	2.20	0.15	—	—	—	Died
7	0.47	1.87	1.45	0.16	0.77	—	0.54	Alive
8	0.42	5.09	0.72	1.25	—	1.14	0.72	"
9	0.82	2.84	2.55	1.59	0.06	—	—	Died
10	0.15	0.49	2.09	0.07	—	—	—	Died
11	0.66	2.23	0.17	—	—	—	—	Died
Control experiments								
12	0.68	0.60	0.63	0.65	0.64	0.65	0.66	No reaction
13	0.32	0.31	0.31	0.32	0.30	0.34	—	

[1] Serum, 2 ml per 1 kg body weight, administered for the first time.

known that during these days changes of excitability and functional mobility of peripheral neuromuscular formations are particularly marked [5] as are disturbances of the dynamics of the main nervous processes – excitation and inhibition – at the highest levels of the central nervous system [3, 8]. It could be taken, in connection with the data cited, that the observed changes in blood bromine concentration could be determined by changes in the functional state of the nervous system in protein sensitization.

The most marked and consistent changes in blood bromine content were observed during anaphylactic shock. Phasic disturbances of nervous activity were, as a rule, accompanied by biphasic fluctuations in the blood bromine level. As can be seen from Table 2, if there was accummulation of bromine in the blood, sometimes reaching high values (2.88-3.61-5.09 mg%), during the first few minutes after the booster injection of serum then subsequently, as the torpid phase of shock developed and deepened, the blood bromine level passed to the second phase – the phase of gradual diminution.

It must be emphasized that in all cases of anaphylactic shock with fatal outcome, hypobromemia was found a few minutes before death, while in cases of survival the blood bromine level during anaphylactic shock remained raised, to a greater or lesser extent, as compared with the initial level; this continued for $1\frac{1}{2}$-2 hours after administration of the booster dose of serum (see Fig).



Changes in blood pressure and respiration after booster injection of serum (Experiment 11). Records (from above down): respiratory movements, blood pressure in the femoral artery, base line and signal of serum injection. Time marker (2 seconds). A) Normal, B) 15 minutes after repeat injection.

During the postshock period no consistent fluctuations in the blood bromine level could be observed: in 2 dogs hypobromemia was still noted 20 days later, while in 3 others the blood bromine level was similar to the initial level within the first 24 hours after shock.

The present material indicates that the appearance and development of the anaphylactic state is accompanied by changes in blood bromine content. Phasic disturbances of nervous activity during anaphylactic shock evidently determined the biphasic fluctuations of the blood bromine level. The findings concerning the biphasic changes in the blood bromine content after the booster injection of serum can be tentatively explained on the assumption that at thebeginning of shock bromine passes from most of the tissues into the blood and is then transferred to other organs, including the central nervous system where bromine is known to favor enhancement and concentration of inhibitory processes. From this point of view, the hypobromemia observed during the first few minutes following the booster administration of serum may be regarded as a defensive reaction of the organism against the "excessive stimulus," viz. antigen.

SUMMARY

In the majority of cases of protein sensitization in dogs, beginning from the 8th to the 12th day following the introduction of the first sensitizing dose, there was a general tendency of the blood bromine level to decrease. Besides, from the 18th to the 22nd day – the last days of sensitization – there was relative instability of the blood bromine level. Variations of the latter during anaphylactic shock were of a biphasic character, i.e., hyperbromemia at the onset of shock was replaced by gradual reduction of the bromine level which sometimes

fell to marked hypobromemia. The latter was especially pronounced in animals which died within the first hour after the introduction of the booster of the serum.

No regular deviations in the blood bromine content were revealed in the postshock period.

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