

Preliminary (before ischemia for 2 h) injection of TP and L caused constriction of the cisterns of the RER, as a result of which the bulk density of RER was reduced by 31-39% compared with the control. The surface area of the RER membranes remained unchanged in this case (Fig. 1a). Prophylactic injection of TP and L led to preservation of the structural organization of the SER, except during the initial period of recirculation (after restoration of the blood flow for 2 h), when the bulk and surface densities of SER were reduced (Fig. 1b).

Prophylactic combined administration of the antioxidant TP and the phospholipase inhibitor L thus had a marked anti-ischemic effect, and reduced the severity of the postischemic structural and functional changes in the liver.

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EFFECT OF ALCOHOL POISONING ON LEVELS OF ANTIBODIES TO CATECHOLAMINES AND SEROTONIN IN ANIMALS DIFFERING IN PREDISPOSITION TO EXPERIMENTAL ALCOHOLISM

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It was shown previously [3] that chronic alcohol poisoning in animals predisposed to develop experimental alcoholism is characterized by strengthening of the immune response to sheep's red blood cells (SRBC) and by hypoactivity of SRBC-induced T suppressor cells, whereas in animals rejecting alcohol, on the other hand, depression of antibody formation and hyperactivity of antigen-specific and concanavalin A-induced T suppressor cells are observed. Evidence of the formation of antibodies to catecholamines and serotonin (5-HT) in pathological

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TABLE 1. Levels of Anti-NA and Anti-5-HT Antibodies in Different Lines of Mice with Chronic Alcohol Poisoning ($M \pm m$)

Line of mice	Experimen- tal condi- tions	Number of ani- mals	Antibodies to NA			Antibodies to 5-HT		
			duration of alcohol poisoning, months					
			1	3	10	1	3	10
C57Bl/6	Experiment	24	0	14,6±3,8*	0	0	15,6±4,2*	0
	Control	24	0	1,3±0,6	3,3±1,9	0	2,0±0,9	1,0±0,2
DBA/2	Experiment	18	0	1,2±0,3	0	0	1,3±0,4	0
	Control	18	0	0	2,0±0,3	0	0,66±0,2	1,0±0,2
CBA	Experiment	12	0	0	—	0	0	—
	Control	12	0	0	—	0	0	—

Legend. $*p < 0.05$.

states accompanied by disturbance of metabolism of biogenic amines, has recently been obtained [5, 6].

Since an essential role in the mechanisms involved in the formation of chronic alcoholism is played by disturbances of the catecholamine- and serotonergic neurotransmitter systems [1, 2], it was decided to attempt to discover antibodies to noradrenalin (NA) and 5-HT in mice of different lines, characterized by differences in their predisposition to develop experimental alcoholism, with chronic experimental alcohol poisoning.

EXPERIMENTAL METHOD

Experiments were carried out on 140 male C57BL/6, CBA, and DBA/2 mice weighing initially 16-18 g. C57BL/6 mice are characterized by predisposition to develop experimental alcoholism, whereas CBA and DBA/2 mice refuse to take alcohol [7]. To produce chronic alcohol poisoning, the mice were given 15% ethanol solution to drink instead of water for 10 months. Levels of anti-NA and anti-5-HT antibodies in the blood serum were determined at different periods of alcohol administration to the animals, 1, 3, and 10 months after the beginning of the experiment.

Concentrations of anti-NA and anti-5-HT antibodies were determined by the passive hemagglutination test (PHT), using SRBC, covalently bonded with NA or 5-HT [8] as diagnostic serum. The specificity of the antibodies discovered was verified by the passive hemagglutination inhibition test (PHIT) with NA and 5-HT in a concentration of 4 mg/ml. The antibody level was expressed in conventional units. The minimal quantity of antibodies causing agglutination was taken to be 1 conventional unit. The antibody concentration was calculated by the formula $T^{-1} - H^{-1}$, where T is the antibody titer in the PHT and H the antibody titer in the PHIT.

The numerical results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Data on levels of anti-NA and anti-5-HT antibodies in mice characterized by differences in predisposition to ethanol, in the course of chronic alcohol poisoning, are given in Table 1. Antibodies to NA and 5-HT were discovered in levels higher than 10 conventional units in the blood serum only of C57BL/6 mice, at the 3rd month of chronic alcohol poisoning. They were not found in the blood serum in the 1st and 10th months of poisoning of the mice with alcohol. In CBA and DBA/2 mice either no antibodies were found or their levels were below 3 conventional units.

The experiments thus showed that after alcohol poisoning for 3 months antibodies to NA and 5-HT were found in the blood serum of C57BL/6 mice, a line characterized by predisposition to develop experimental alcoholism, whereas either no antibodies were found, or they were found in very small quantities, in DBA/2 and CBA mice, which reject alcohol. Similar results were obtained in a study of antibody formation to SRBC in mice of different lines, differing in their predisposition to alcohol consumption [3]. On the one hand, the appearance of antibodies to neurotransmitters during alcohol poisoning may be connected with a profound disturbance of biogenic amine metabolism in this pathology, leading to the formation of reactable compounds in the body, forming conjugate antibodies with proteins, to which specific antibodies are formed [6]. In the present case antibodies to NA and 5-HT perform

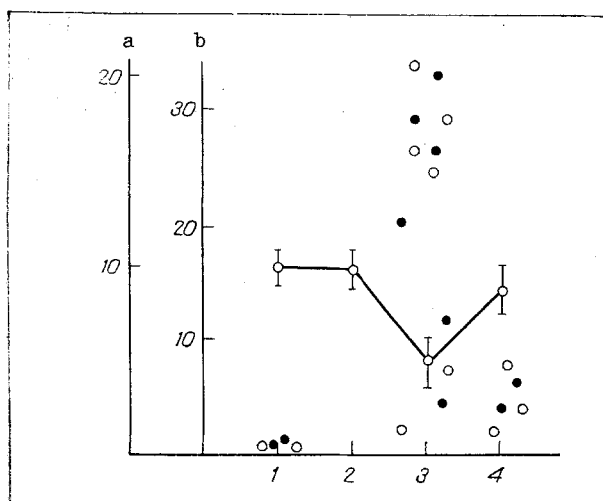


Fig. 1. Ethanol consumption by C57BL/6 mice during period when antibodies to 5-HT (empty circles) and to NA (filled circles) appear in the blood. Abscissa, time (in months); ordinate: a) ethanol consumption (in g/kg), b) level of antibodies to NA and 5-HT (in conventional units).

an adaptive function, correcting the defect in metabolic mechanisms leading to accumulation of an excess of products of biogenic amine metabolism. On the other hand, it can be postulated that antibodies to NA and 5-HT may exert an influence at the level of alcohol motivation in animals. To examine this hypothesis, a special experiment was carried out in which the free consumption of alcohol was studied in C57BL/6 mice for 4 months. The level of free alcohol consumption was determined daily for 4 months, under conditions of choice between 15% ethanol solution and water, by recording the quantity of alcohol drunk. It was found that C57BL/6 mice consume significantly less 15% alcohol solution in the 3rd month of free consumption of ethanol than at other times of observation (Fig. 1). Meanwhile, the highest production of antibodies to NA and 5-HT was recorded at that time in the animals' blood serum.

It thus follows from these experiments that animals in whose blood serum anti-nor-adrenalin and anti-serotonin antibodies were found drank smaller quantities of ethanol, i.e., alcohol motivation in these animals was reduced. This hypothesis is confirmed by previous data [4] relating to immunization of C57BL/6 mice with 5-HT conjugates. It was shown that in the case of artificial formation of antibodies to 5-HT, alcohol motivation is reduced. In all probability antibodies to neurotransmitters formed in the body chronic alcohol poisoning exert a protective action, modify alcohol motivation in animals and, in that way, prevent the formation of physical dependence on alcohol.

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