Disturbances of bile production are much less severe after repetition of the resection, and restitution of normal biliary function takes place much sooner.

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EFFECT OF THE DRUG TETAMON-I ON THE BILE SECRETING FUNCTION OF THE LIVER

N. P. Skakun and A. Ya. Sereda

From the Chair of Pharmacology (Director: Assistant Prof. Yu. A. Petrovsky), Lvov State Medical Institute (Director: L. N. Kuzmenko)

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We showed in our previous communication [10] that Difenin, which hinders transmission of nerve impulses in N-cholinergic systems, exerts a marked inhibitory effect on the biliary function of the liver.

The present paper deals with the nature of the effect of Tetamon-I (tetraethylammonium iodide) on bile formation in the liver.

As has been shown by the work of K. M. Bykov, A. V. Rikkl , E. P. Ivanov, and S. L. Balakin [4, 5, 7, 9] and others, bile secretion is under the control of the central nervous system, and disturbances of the nervous connections between the central nervous system and the liver should lead to alterations in hepatic function.

Tetraethylammonium derivatives inhibit transmission of impulses in N-cholinergic systems of peripheral ganglions, chiefly of the parasympathetic system [1, 2, 3, 6, 8, 11].

EXPERIMENTAL METHODS

The experiments were performed on 4 dogs provided with permanent gall-bladder fistulae, and with ligated common bile ducts. Each experiment lasted 4 hours, and we determined the amount of bile secreted, and its bile acid content, for each hour. In the first series of experiments we examined the effect of Tetamon-I on spontaneous bile secretion, and in the second series we examined the effect during digestion. The injections of the drug were followed immediately by breakfast, consisting of 250 ml of milk and one large hen's egg. Tetamon-I was injected intravenously (in some experiments intramuscularly), in doses of 0.5-2 ml, corresponding to

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* In Russian.

3.3-14 mg per kg body weight. In all, we performed 44 experiments.

TABLE 1

Effect of Tetamon-I on Flow of Bile in Dogs

Dog	Amount of bile, in ml										
	before injection of drug					after injection of drug					
	1 hr.	2 hrs.	3 hrs.	4 hrs.	total for 4 hrs.	dose in mg/kg	1 hr.	2 hrs.	3 hrs.	4 hrs.	total for 4 hrs.
a) For spontaneous flow of bile											
Mukha	7.3	8.7	10.3	9.5	35.8	7.0	6.9	4.9	11.2	8.9	31.9
	7.3	8.7	10.3	9.5	35.8	14.0	4.4	6.4	11.2	8.9	30.9
Alfa	9.3	9.2	9.5	10 3	38.3	6.3	6.5	5.7	5.8	7.3	25.3
Kashtanka	12.1	12.1	10.7	7.5	42.4	3.3	13.8	10.6	7.8	8.0	40.2
	12.1	12.1	10.7	7.5	42.4	6.6	7.8	6.9	7.4	7.3	29.4
b) For flow of bile during digestion											
Sultan	6.5	6.9	8.0	10.0	31.4	5.0	2.7	6.0	9.0	7.3	25.0
Mukha	6.5	9.3	7.9	12.2	35.9	7.0	3.5	6.6	10.0	11.2	31.3

EXPERIMENTAL RESULTS

As is evident from Table 1, administration of Tetamon-I in most cases caused a reduction in the spontaneous flow of bile. The amount of bile produced by the dog Mukha after intravenous injection of 1 ml of the drug (7 mg per kg body weight) fell by about 11% over 4 hours, and after 2 ml of the drug by 13.7%. The effects were more marked in the dogs Alfa (diminution in flow of 34% after a dose of 6.3 mg per kg body weight), and Kashtanka, in which a dose of 6.6 mg per kg body weight lowered bile secretion by 30.7%. No changes were seen in the dog Kashtanka after injection of half this dose (3.3 mg per kg body weight). Inhibition of bile secretion took place chiefly during the first two hours after injection, with subsequent rise to the normal level.

At the same time, we observed changes in the composition of the bile, in particular, a regular fall in the bile acids content, which was evident over the entire 4 hours of observation (Table 2).

Determination of the total bile acid content showed that this had diminshed by 30-40% for spontaneous flow of bile. Depression of bile acid secretion was particularly evident during the first two hours of action of the drug.

Similar results were obtained in experiments on the effect of Tetamon-I on bile secretion during digestion. The flow fell by 12.5-20.4%, for the dogs Sultan and Mukha, and the bile became much more dilute, with a fall in the content of bile acid salts of 22.5-42%.

It thus appears that the effect of tetraethylammonium iodide (Tetamon-I) is to lower the amount of bile produced, and to reduce the concentration of its chief component, the bile acids. This is evidence of depression of the biliary function of the liver, inasmuch as synthesis of bile acids is a specific function of the liver.

It can only be assumed that this effect is due to the hindrance of transmission of nerve impulses in N-cholinergic systems, mostly of the parasympathetic ganglions, by tetraethylammonium salts.

TABLE 2

Effect of Tetamon-I on the Bile Acid Content of the Bile

Dog	Content of bile acid salts in the bile, in mg-%										
	before injection of drug					after injection of drug					
	1 hr.	2 hrs.	3 hrs.	4 hrs.	total for 4 hrs.	dose in mg/kg	1 hr.	2 hrs.	3 hrs.	4 hrs.	total for 4 hrs.
a) For spontaneous flow of bile											
Mukha	3 280	3 460	2 840	3 210	1 137.9	7.0	2 670	2 620	2 330	2 080	791.2
	3 280	3 460	2 840	3 210	1 137.9	14.0	3 000	2 080	2 620	2 540	784.6
Alfa	1 920	2 000	1 920	1 910	741.7	6.3	1 990	1 820	1 580	1 670	446.0
b) For flow of bile during digestion											
Sultan	4 880	4 840	4 620	4 440	1 464.8	5.0	4 230	3 930	2 960	3 210	850.7
Mukha	2 850	2 430	2 300	2 310	874.8	7.0	2 540	2 340	2 180	1 930	677.5

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