Effect of Biliary Stimulants on Disappearance Rate of Intravenously Administered Cholesterol. (17764)

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This investigation studied the effects of biliary salts (Bilron-Lilly and sodium dehydrocholate), on the removal of intravenously administered cholesterol from the blood stream in rabbits. All of the animals were given 100 mg of cholesterol per kg intravenously. Plasma containing 3000 mg % of cholesterol or more, which was obtained from rabbits previously fed cholesterol, was used as the source of cholesterol according to the procedure employed by Horlick, Feldman and Katz(1). The rabbits were divided into 3 groups, one serving as the control, the others receiving either Bilron or sodium dehydrocholate in amounts indicated in the table. This was administered at the same time as the hypercholesteremic and hyperlypemic plasma and repeat doses were given 24 and 48 hours later. Total and free serum cholesterols were determined by the Schoenheimer-Sperry(2) method on samples taken before the injection and at intervals of 15 minutes, 24, 48 and 72 hours later. As shown in the Table I no significant effect was noted on the disappearance rate of the injected cholesterol following the administration of the test drugs. Since these bile salts, especially Bilron, increase the 24 hour biliary cholesterol excretion it may be

TABLE I.

Control* Cholesterol		15 min Cholesterol		24 hr Cholesterol		48 hr Cholesterol		72 hr Cholesterol		Hematocrit
Total	Free	Total	Free	Total	Free	Total	Free	Total	Free	fall§
I. Sodium Dehydrocholate.†										
91	39	205	83	178	71	145	63	150	57	9
50	19	238	70	122	31	84	33	90	40	8
69	25	255	100	128	33	128	44	122	48	8
55	21	205	83	97	21	99	55	134	77	7
43	23	248	92	111	36	107	40	113	42	7
II. Bilron.‡										
66	44	263	68	68	44	Not taken		150	71	5
73	36	275	75	127	68			153	63	4
73	22	295	94	108	44	Expired 40 hrs				
81	40	256	88	104	48	109	59	159	75	
68	30	248	82	111	47	113	52	142	53	1
90	42	266	92	132	59	110	46	110	38	5
45	31	186	63	73	37	89	30	111	33	1
III. Control Rabbits.										
40	25	220	70	125	55	—	75	160	80	4
60	40	230	80	150	75	80	45	70	40	6
80	25	280	85	120	48	90	55	100	65	3
70	50	260	90	110	55	95	48	80	60	4
70	50	260	93	170	90	120	45	90	45	3

* Cholesterol (100 mg/kg) inj. intrav. together with test drug immediately after withdrawal of control sample.

† All rabbits given sodium dehydrocholate intrav. with equal repeat doses at 24 and 48 hr; total, 2 g.

‡ Rabbits No. 1-3 given Bilron (Lilly) by stomach tube, with equal repeat doses at 24 and 48 hrs; total, 2 g. Rabbits No. 4-7 same as † but total 2.6 g.

§ Fall in hematocrit between control and 72-hr samples.

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concluded that the removal of intravenously administered cholesterol was not significantly accelerated by either this mechanism or by any possible more direct action of these substances on cholesterol metabolism.

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Platelet Regeneration During Therapy of Acute Leukemia with Folic Acid Antagonists.* (17765)

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Temporary remissions in acute leukemia have been produced by the therapeutic administration of the various folic acid antagonists. Observations have varied as to the response of the blood platelets. Farber *et al.*(1,2) reported improvement in the platelet level in some of his cases. Dameshek(3) in a preliminary report stated that a definite increase in blood platelets must be considered as a part of the criteria in determining whether or not a remission had occurred but no other data are given. Meyer *et al.*(4) observed no significant effect on the platelet level of patients with acute and chronic leukemia treated with aminopterin (4-amino, pteroyl glutamic acid). Berman *et al.*(5) reported no regular response in platelets in nine cases of chronic leukemia treated with aminopterin. Stickney *et al.*(6) merely state that the platelets may increase in number during remissions. Sacks *et al.*(7) reported his findings in 14 cases of acute leukemia and in 4 cases with an initial thrombocytopenia a definite platelet response occurred.

In a series of 48 patients (children and adults) with acute leukemia of all types treated with folic acid antagonists, results were obtained which indicated that when a definite remission occurred the elevated platelet response was a part of the hematologic and clinical improvement. In the cases presented the regeneration of platelets and other formed elements of the peripheral blood followed a rather set pattern not mentioned in previous publications.

Experimental. The following folic acid antagonists were used: 4-amino, pteroyl glutamic acid (aminopterin); 4-amino, N^{10} methyl pteroyl glutamic acid (a-methopterin); 4-amino, pteroyl aspartic acid (amino-an-fol); nd 4-amino, 9 methyl pteroyl glutamic acid (a-ninopterin). These antagonists were administered intramuscularly or orally in approximately the same dosages as recommended by Farber(1,2) and Dameshek(3). Platelet levels were determined by the Rees-Ecker method, normal values in our laboratory being 225,000 to 325,000 per cu mm. The hemoglobin, red cell levels, leukocyte counts and differential counts were also frequently done in addition to bone marrow biopsies by the aspiration method. The leukocytes were studied qualitatively by the supravital method using Janus green and neutral red.

Observations. A definite response, either

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