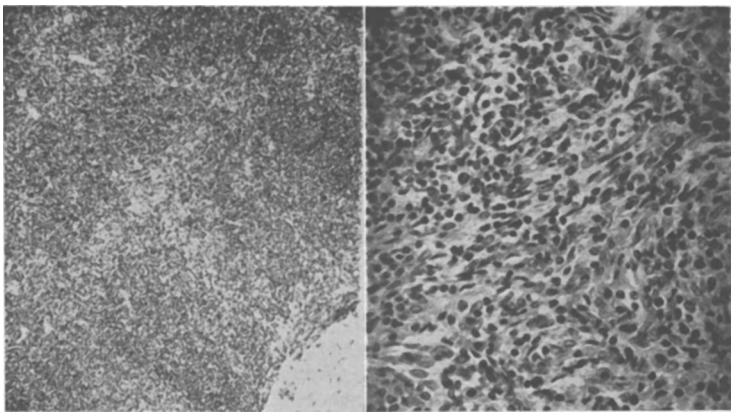

FIG. 5 and 6. ×50 and ×200. Lymph node from guinea pig 24 hr after inj. with 5 cc of serum from a patient with monocytic leukemia.

groups." The nodes from the animals that received sera from normal individuals showed on the whole nothing unusual.

The sera of patients with chronic myeloid leukemia bring about changes similar to those ascribed to cortisone itself or as initiated in action by ACTH in so far as the lymph node change is concerned. Myelokentric acid brings about similar lymph node changes and, as does cortisone, it also brings about increases in erythropoiesis, myelo-leukopoiesis and platelet formation. We do not, however, believe that it is cortisone.

The increased lymphopoiesis in the lymph nodes of animals that received serum from patients with chronic lymphoid leukemia is similar to that which we have described in animals that have received lymphokentric acid in urinary extracts.

It would seem then that at least 2 and possibly 3 pathologic pictures may be made out in the nodes of these animals. This would seem to indicate that there are substances in the blood of these patients that are probably conjugates of myelokentric and lymphokentric acid. The presence of these may be detected in the sera of patients with lymphomatoid disease by bioassay. It also strengthens our contention that these are humoral hormones.

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Variations in Serum Cholesterol of Normal Rabbits after Injection of Hypercholesterolemic Rabbit Plasma. (18289)

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Investigators have long been interested in producing atherosclerosis by intravenous injection of cholesterol suspensions. Dewey(1), Fitz and Bruger(2), Bevans(3) and Pollak (4) have reported their experience with colloidal solutions of free cholesterol. The present experiments were carried out to de-

1. Dewey, K., *Arch. Int. Med.*, 1916, v17, 757.

2. Fitz, F., and Bruger, M., *J. Biol. Chem.*, 1936, v114, xxxv.

3. Bevans, M., *Am. J. Med.*, 1949, v6, 103.

4. Pollak, O. J., *Am. Heart J.*, 1949, v38, 455.

TABLE I. Control Group.

Exp. No.	Experiment	Chol. fraction	Time 0	5 min.	15 min.	30 min.	60 min.	2 hr	4 hr	6 hr	24 hr	48 hr
1	20 ml normal rabbit plasma containing 13 mg cholesterol. Fasting 0 to 24 hr	T.	75	56	67	68	72	63	63	61	102	106
		E.	46	35	42	42	45	40	42	38	64	63
		F.	29	21	25	26	27	23	21	23	38	43
		E/F	1.6	1.7	1.7	1.6	1.7	1.7	2.0	1.7	1.7	1.5
2	20 ml normal rabbit plasma containing 7 mg cholesterol. Fasting 0 to 24 hr	T.	66	61	61	62	59	58	58	59	78	
		E.	44	40	41	43	41	40	40	40	50	
		F.	22	21	20	19	19	17	18	19	29	
		E/F	2.0	1.9	2.1	2.2	2.2	2.3	2.2	2.1	1.7	
3	20 ml normal rabbit plasma containing 5 mg cholesterol. Fasting 0 to 24 hr	T.	38	35	30	30	25	25	24	25	30	
		E.	27	22	22	22	18	17	16	17	19	
		F.	11	12	9	8	7	8	8	8	11	
		E/F	2.4	1.8	2.6	2.9	2.4	2.1	2.0	2.2	1.8	
4	20 ml normal saline. Fasting 0 to 24 hr	T.	66	60	61	56	52	90	87	88	100	64
		E.	43	37	39	35	32	57	56	56	56	41
		F.	23	24	22	21	21	33	30	32	45	22
		E/F	1.9	1.6	1.8	1.7	1.5	1.7	1.9	1.8	1.2	1.8
5	Nothing given. Non-fasting	T.	65	59	59	54	66	65	65	54	75	65
		E.	37	37	30	26	38	41	37	26	27	35
		F.	28	23	28	28	27	24	28	28	48	30
		E/F	1.3	1.6	1.1	0.9	1.4	1.7	1.3	0.9	0.6	1.2

T = Total cholesterol mg/100 ml.
E = Esterified cholesterol mg/100 ml.
F = Free cholesterol mg/100 ml.
E/F = Esterified cholesterol/free cholesterol.

termine the effect of the intravenous administration of hypercholesterolemic rabbit plasma on the free and total serum cholesterol of normal rabbits.

Procedure. Hypercholesterolemic plasma was obtained by cardiac puncture from male rabbits, 3 to 6 months old, which were fed 3 g of cholesterol per week for 8 weeks or longer. The recipient animals were male rabbits of the same age group which received no cholesterol in their diet. The control group consisted of 5 normal male rabbits. In 3, 20 ml of normal rabbit plasma containing an average of 8.3 mg of cholesterol was injected into an ear vein. In one rabbit, 20 ml normal saline was injected and in another, nothing was given by mouth or vein. Specimens of blood were obtained by cardiac puncture in the non-anesthetized state at the following intervals: before injection, 5, 15, 30 and 60 minutes, 2, 4, 6 and 24 hours and at times 48 hours after the injection. Duplicate determinations of the free and total cholesterol in the sera were made by the Schoenheimer-Sperry method(5). In the experimental group, each of 4 normal male rabbits was injected intravenously with 20 ml of plasma containing an average of 132 mg of cholesterol. Blood specimens were obtained and examined in the same manner as in the control group.

Results. Table I presents the data obtained in the control experiments. It will be noted that the injection of normal rabbit plasma containing a small amount of cholesterol had little effect on the total cholesterol or E/F ratio for 6 hours. In 24 hours, however, the total cholesterol increased significantly in 2 experiments (Exp. 1 and 2). The same results were obtained when 20 ml normal saline were injected into the ear vein or when nothing was given parenterally or by mouth. Table II presents the data obtained in the experimental studies. The total serum cholesterol increased rapidly after the injection, the highest values being obtained in the 5 minute specimen. Thereafter, the serum cholesterol fell gradually, the lowest value being obtained in 6 hours or less. In 24 hours, the total serum cholesterol was significantly increased above the 6 hour level as in the control group. The E/F ratio was

5. Schoenheimer, R., and Sperry, W. M., *J. Biol. Chem.*, 1934, v106, 745.

TABLE II. Experimental Group.

Exp. No.	Experiment	Chol. fraction	Time 0	5 min.	15 min.	30 min.	60 min.	2 hr	4 hr	6 hr	24 hr	48 hr
1	20 ml rabbit plasma containing 130 mg cholesterol. Non-fasting	T.	59	162	151	145	129	97	74	74	101	94
		E.	33	102	101	96	82	57	44	44	57	50
		F.	26	60	50	49	47	40	30	30	44	45
		E/F	1.3	1.7	2.0	2.0	1.8	1.4	1.4	1.5	1.3	1.1
2	20 ml rabbit plasma containing 133 mg cholesterol. Fasting 0 to 24 hr	T.	52	187	180	174	148	123	97	70	96	
		E.	28	118	117	110	86	76	54	35	51	
		F.	24	69	64	65	62	48	43	35	45	
		E/F	1.2	1.7	1.8	1.7	1.4	1.6	1.3	1.0	1.1	
3	20 ml rabbit plasma containing 130 mg cholesterol. Fasting 0 to 24 hr	T.	49	153	145	138	104	69	70	70	84	
		E.	35	105	102	98	72	45	48	46	54	
		F.	14	48	43	39	32	24	22	25	30	
		E/F	2.5	2.2	2.4	2.5	2.3	1.8	2.2	1.9	1.8	
4	20 ml rabbit plasma containing 135 mg cholesterol. Fasting 0 to 24 hr	T.	60	205	197	161	154	138	94	85	108	

not altered significantly.

Discussion. Bevans(3) noted a secondary rise in total serum cholesterol but not in free cholesterol in rabbits 24 hours after the intravenous injection of 0.5 g of a colloidal solution of free cholesterol. She interpreted this to be due to clearing of the injected cholesterol from the blood and a slow return after esterification. In the experimental group, here reported, an increase in the total serum cholesterol occurred in 24 hours. A secondary rise in the free cholesterol must have occurred simultaneously since there was no change in the E/F ratio. The variation of these results from those reported by Bevans may be explained by the fact that hypercholesterolemic plasma containing free and esterified cholesterol was injected in these experiments. In the control experiments, however (Table I), an increase in the total serum cholesterol was also noted in 24 hours after the injection of normal rabbit plasma, normal saline or when nothing was given. The rise in total serum cholesterol is therefore not an intrinsic response to the injection of cholesterol as reported by Bevans but apparently is related to the mechanics of performing the experiment, *i.e.*, the result of serial blood letting and/or trauma.

Summary. The intravenous administration of hypercholesterolemic rabbit plasma in normal rabbits resulted in a rapid increase in total serum cholesterol followed by a gradual decrease. The highest value was obtained in 5 minutes and in 6 hours or less the total serum cholesterol had reached the lowest post-injection level. In 24 hours, the total serum cholesterol was significantly increased above the 6 hour level with no significant alteration in the E/F ratio. Rabbits receiving normal rabbit plasma, normal saline or no injection showed little alteration in the total serum cholesterol for 6 hours. In 24 hours, the total serum cholesterol likewise increased significantly compared to the 6 hour level. The rise in total cholesterol at 24 hours is apparently related to the mechanics of performing the experiment rather than to the injection of cholesterol.

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