

Prevention of Cholesterol Arteriosclerosis in the Rabbit by Use of Pancreatic Extract (Lipocaic).

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Dragstedt, Van Prohaska and Harms¹ reported observations on a substance present in pancreas which permits survival and prevents liver changes in depancreatized dogs. To this substance they gave the name "Lipocaic". The interesting effects of this substance on lipid metabolism led us to investigate its effect on the atherosclerosis which can be produced in rabbits by feeding cholesterol and foods high in cholesterol content. This experimental vascular change in rabbits has been studied particularly by Anitschkow,² Bailey,³ Clarkson,⁴ Dominguez,⁵ and Duff.⁶

Lipocaic was prepared according to the method of Dragstedt, Van Prohaska and Harms.¹ The procedure involves the extraction of fresh pancreas with 60% ethyl alcohol. The alcohol extract is then evaporated at a temperature less than 40°C. The residue is extracted with sulphuric ether. The fat-free extract dissolved in water was so diluted that 5 cc. contained the extract of 50 gm. of pancreas.

In this study, the diet fed to all the rabbits consisted of a standard ration of oats, Purina rabbit chow and green vegetables. Each rabbit receiving the high cholesterol diet was given each morning one 50 cc. beaker of this chow containing 0.5 gm. cholesterol and one-half egg yolk. No difficulty was experienced in making the animals eat this mixture. After eating this, they were given additional food.

In the case of the hormone, the preparation of which was described above, 5.0 cc. of the concentrated watery substance containing the extract obtained from 50 gm. of pancreas was added to a 50 cc. beaker of Purina rabbit chow. Each rabbit receiving the hormone was given one of these beakers of chow daily.

¹ Dragstedt, L. R., Van Prohaska, J., and Harms, H. P., *Am. J. Physiol.*, 1936, **117**, 175.

² Anitschkow, N., *Beit. z. Path. Anat. u. z. Allg. Path.*, 1913, **56**, 379.

³ Bailey, C. H., *J. Exp. Med.*, 1916, **23**, 69.

⁴ Clarkson, S., and Newburgh, L. H., *J. Exp. Med.*, 1926, **43**, 595.

⁵ Dominguez, R. J., *Exp. Med.*, 1927, **46**, 463.

⁶ Duff, G. L., *Arch. Path.*, 1935, **20**, 81, 259.

TABLE I.
Prevention of Cholesterol Arteriosclerosis in the Rabbit by Use of the Pancreatic Hormone Lipocaine.

Rabbit No. Weeks	Blood Cholesterol, mg. per 100 cc.													Group VI Rabbit No. 16 Received Balanced Diet and Choles- terol for Ten Weeks, then Cholesterol Was Discontinued							
	Group I Received Balanced Diet			Group II Received Lipocaine and Balanced Diet			Group III Received High Cholesterol and Balanced Diet			Group IV Received High Cholesterol Balanced Diet and Lipocaine			Group V Rabbit No. 14 Received Balanced Diet, Choles- terol, and Lipocaine Heated to 90° C.			Group V Rabbit No. 15 Received Balanced Diet, Choles- terol and Lipocaine Heated to 65° C.					
	1	2	3	4	5	6	7	8	9	10	11	12	13		10	11	12	13	10	11	12
0	74	25	87	80	21	109	33	47	31	72	51	64	25	48	48	48	25	48	48	48	48
1	84	56	64	93	34	97	152	235	21	92	58	56	44	43	43	43	44	43	43	43	292
2	76	56	83	87	33	87	265	334	63	59	43	74	37	58	58	58	37	58	58	58	309
3	77	37	55	70	38	94	640	606	56	68	51	91	847	292	292	292	847	292	292	292	334
4	72	38	78	98	33	74	670	658	50	55	59	62	889	376	376	376	889	376	376	376	494
5	67	36	69	94	69	73	740	904	47	81	83	67	1107	455	455	455	1107	455	455	455	633
6	76	47	131	71	30	77	1017	1085	75	64	79*	83	1187	474	474	474	1187	474	474	474	708
7	64	34	94	68	21	104	1026	494	37	93	177	76	1474	555	555	555	1474	555	555	555	808
8	56	51	97	49	43	91	1105	684	51	89	278	56	1389	546	546	546	1389	546	546	546	952
9	60	39	73	45	37	119	1220	989	56	79	281	92	1333	591	591	591	1333	591	591	591	1085
10	71	47	101	55	40	96	1290	1250	58	92	303†	89	1275	658	658	658	1275	658	658	658	1135
11							1666	1666													
12			82			94					204	77									993
13			85			101					167	111									705
14			77			123					108	104									658
15			68			108					121	99									593
16			75			112					81	119									581
17																					
18																					
19																					
20																					
Autopsy Findings																					
Gross																					
Atherosclerosis																					
of Aorta																					
Microscopic																					
Atherosclerosis																					
of Aorta																					

*Bottled hormone substituted after this cholesterol determination. †Unheated hormone treatment resumed.

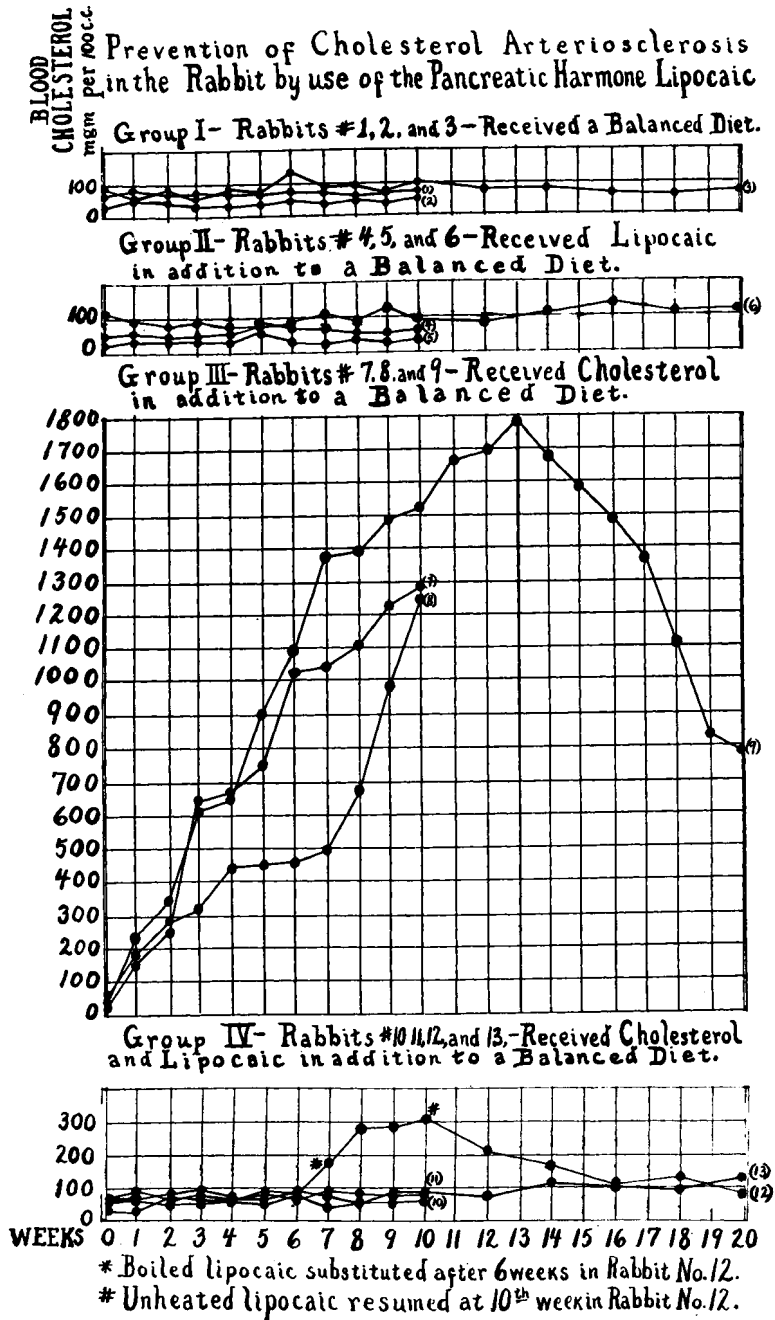


CHART 1.

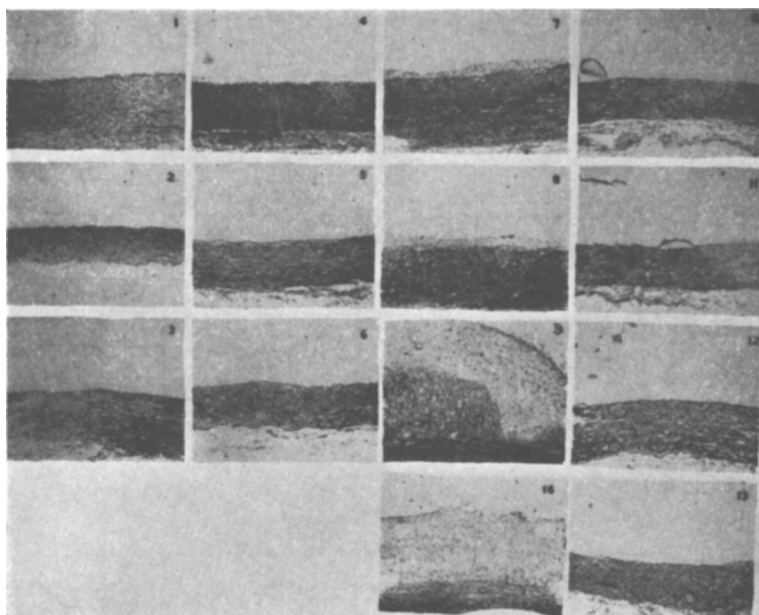
All animals used in this experiment were approximately 6 months of age at the beginning of the experiment. Rabbits Nos. 3, 6, and 13 were from one litter, and Nos. 11, 12, and 16 from another litter.

The procedures carried out in the six groups of rabbits are described in Table I.

Weekly determinations of blood cholesterol were done according to a modification of the method of Bloor.⁷

The feeding experiment continued for 10 weeks after which Rabbits 1, 2, 4, 5, 7, 8, 10, 11, 14, and 15 were sacrificed and an autopsy done. Rabbits 3, 6, 9, 12, 13, and 16 were observed for a period of 20 weeks and then sacrificed and an autopsy done. Gross and microscopic studies were made of the vascular system and organs of all animals.

The effects of the administration of lipocaic are evident both in the changes in blood cholesterol and in the gross and microscopic appearance of the aorta of the rabbits at an autopsy.



Rabbits 1, 2, and 3 received balanced diet.

Rabbits 4, 5, and 6 received balanced diet and lipocaic.

Rabbits 7, 8, 9, and 16 received balanced diet and cholesterol.

Rabbits, 10, 11, 12, and 13 received balanced diet, cholesterol and lipocaic.

CHART 2.

⁷ Bloor, W. R., *Quant. Clin. Chem.*, 1932, **2**, 884.

The results are shown in Table I. The blood cholesterol changes in the first 4 groups of animals are graphically illustrated in Chart 1. The microscopic appearance of the aorta of the experimental animals 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 16 is shown in Chart 2.

Lipocaic does not affect the level of blood cholesterol in normal animals. It prevents the rise in blood cholesterol and the development of atherosclerosis in the aorta which otherwise regularly occurs in rabbits fed a high cholesterol diet. Heated hormone is ineffective.

Studies are in progress concerning the use of lipocaic in the treatment of atherosclerosis in rabbits in whom the condition has been allowed to develop. The resemblance of cholesterol atherosclerosis of rabbits to the pathology of sclerotic vascular disease in man suggests the possibility of the use of this pancreatic extract in the prevention and treatment of human atherosclerosis.

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Synaptic Connections in the Celiac Ganglia.

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The distribution of axons effecting synaptic connections in the celiac ganglia and their modes of termination have been studied in silver preparations of human material and material obtained from normal and experimental animals (cats). The synapses observed involve (1) pericellular and peridendritic nests, (2) arborizations of axons in dendritic glomeruli, and (3) axon terminations in dendritic fasciculi. Synapses of these types have been described by de Castro¹ in various autonomic ganglia. The synapses effected by the terminal branches of axons with dendrites in dendritic fasciculi probably are the most common in the celiac ganglia. Every ganglion cell in these ganglia probably is synaptically related to more than one axon.

Bilateral section of the splanchnic and vagus nerves and extirpation of the upper lumbar segments of the sympathetic trunks in cats resulted in degeneration of the great majority of the axons which effect synaptic connections in the celiac ganglia but not all of them. Degeneration of only the vagus nerves did not appreciably alter the

¹ de Castro, F., 1931, *Sympathetic Ganglia; Normal and Pathological. Cytology and Cellular Pathology of the Nervous System* (Penfield), Sec. VII.