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Effect of Certain Liquid Organopolysiloxanes on Cholesterol Atherosclerosis of the Rabbit.* (26651)

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It has been postulated that the stability of lipids in emulsion form depends on maintenance of a sufficient surface charge, so that deposition of lipid from plasma at certain sites on the linings of the blood vessels might well result from a lack of surface active agents in plasma(1). Fatty acids are anionic surface active agents and their surface activity is increased by presence of double bonds in the fatty acid radicle(2). Thus, the least saturated fatty acid is the most effective as a charged surface active agent. The pronounced lipemia and cholesterolemia producing effect of a surface active detergent like Triton WR-1339 has been thoroughly explored(3), whereas hydrophobic surface active agents like the silicone fluids have received little attention. Dimethylpolysiloxanes, like DC 200 and DC antifoam,† had only a suggestive effect on aortic atherosclerosis of rabbits(4), but a phenylmethylpolysiloxane‡ altered cholesterol deposition profoundly(5). The present study compares the effect of these 2 silicone fluids in a large number of animals.

Methods and results. In experiments lasting 2 months New Zealand albino rabbits in groups of 6 were fed a stock diet to which 2% cholesterol and .5,% 1%, 2% and 5% of the silicone fluids in weight of diet were added. Weekly serum samples were analyzed for cholesterol by the method of Pearson(6), but the results of the terminal samples only are presented since there were no specific trends in reaching the final value. Tissue cholesterol was determined by the method of Kingsley(7).

The results (Table I) show that the 2 silicone fluids used exert a different biological effect. Addition of phenylmethylpolysiloxane in all concentrations prevents development of severe hypercholesterolemia. The arbitrarily chosen lowest concentration of .5% has as much effect as the 10 times larger amount. The dimethylpolysiloxane did not prevent hypercholesterolemia, except in one experiment where a 1% concentration was used. Even in this instance the effect was less pronounced than that obtained with the other silicone fluid. Cholesterol content of the liver remains esentially unchanged if dimethylpolysiloxane is added to the stock diet containing 2% cholesterol, but increases markedly if the phenylmethylpolysiloxane fluid is fed at the 2% and 5% level. The opposite changes occur in the aorta where the dimethylpolysiloxane produces an increased cholesterol content, whereas addition of phenylmethylpolysiloxane in higher concentrations does not change the cholesterol content of the aorta. The histological lesion of the aorta in a 2% feeding experiment is shown in representative photomicrographs (Fig. 1). Addition of 2% silicone fluids to the stock diet without cholesterol does not alter cholesterol content of the blood serum or of the tissues examined and does not produce histological changes.

Discussion. The cause of the described biological effects of silicone fluids is unknown, therefore the discussion is specula-

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TABLE I. Cholesterol (g %).

	Serum			Liver			Aorta		
	Avg	S.D.	No.	Avg	S.D.	No.	Avg	S.D.	No.
2% cholesterol	1.373	.454	36	2.497	.701	27	.276	.171	27
Idem + .5% DC 200*	1.015	.334	6	1.867	1.022	5	.543	.342	5
" + 1% DC 200	.689	.314	6	—	—	—	—	—	—
" + 2% DC 200	2.084	.230	6	2.672	.515	6	.682	.366	6
" + 5% DC 200	1.855	.763	6	2.123	1.207	6	.669	.653	6
" + .5% XF-10050†	.559	.240	6	2.786	1.160	3	.557	.554	3
" + 1% XF-10050	.412	.138	6	—	—	—	—	—	—
" + 2% XF-10050	.558	.124	12	5.497	1.995	6	.135	.027	6
" + 5% XF-10050	.481	.156	6	3.589	.782	5	.218	.029	5
Stock diet	.073	.019	30	.218	.044	17	.117	.030	23
Idem + 2% DC 200	.090	.034	24	.175	.032	16	.112	.041	11
" + 2% XF-10050	.072	.013	18	.170	.029	10	.083	.048	10

* Dimethylpolysiloxane. † Phenylmethylpolysiloxane.

tive. The original assumption which led to these investigations that the feeding of silicone fluids may change blood surface tension has not been substantiated. Blood surface tension changed proportionally with cholesterolemia, but not with ingestion of silicone fluids(8).

Comprehensive studies on oral feeding of dimethylpolysiloxane in doses as high as 20 g/kg for one month failed to cause discernible effect in rats(9). However, if cholesterol was added to a diet containing 1% dimethylpolysiloxane renal tubular damage was observed in rabbits(4). The present communi-

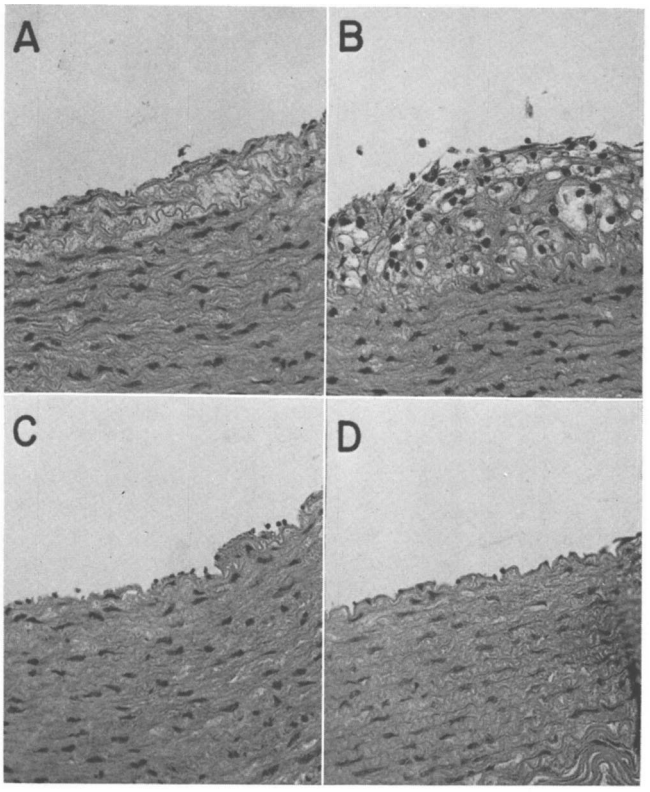

FIG. 1. Aorta of rabbit fed: A, stock diet with 2% cholesterol; B, stock diet with 2% cholesterol and 2% dimethylpolysiloxane; C, stock diet with 2% cholesterol and 2% phenylmethylpolysiloxane; D, stock diet.

cation confirms but does not explain this observation and proliferation of the intima of the aorta containing numerous foam cells (Fig. 1, B) demonstrates the damaging effect of simultaneous feeding of cholesterol and dimethylpolysiloxane. The mechanism by which ingested phenylmethylpolysiloxane prevents severe hypercholesterolemia and the proliferative lesions of the aorta is also obscure, but one may postulate that the phenyl group of this more soluble silicone fluid enhances the transport of triglyceride and cholesterol by the reticuloendothelial system (10).

Summary. Addition of dimethylpolysiloxane to a diet containing 2% cholesterol does not alter hypercholesterolemia and cholesterol content of the liver of rabbits. However, it increases cholesterol content of the aorta and produces atheromatous lesions of the intima. Addition of phenylmethylpolysiloxane to a diet containing 2% cholesterol prevents severe hypercholesterolemia and increases cholesterol content of the liver. It lowers the cholesterol content of the aorta and prevents atheromatous proliferation.

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Estrogen-Progesterone Antagonism on Endometrial Carbonic Anhydrase Activity.* (26652)

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There is ample evidence concerning estrogen-progesterone antagonism in the uterine endometrium. Much has been demonstrated by the histological test based on the proliferative changes in the uterus, the response being rated on the semiquantitative scale. However, little has been done to utilize enzyme determinations in the endometrium as an indicator of hormonal antagonism.

Lutwak-Mann and Adams(1) have studied the effect of stilbestrol on development of progestational activity by the measurements of uterine carbonic anhydrase and progestational proliferation. They observed that in the enzymic test stilbestrol prevented progestational development, and noted that with few exceptions there was good agreement between the enzymic and histological test in evaluating the antagonism.

More recently a work of Miyake and Pincus(2), concerning the antiprogestational activities of estrogens, namely estradiol, estrone, estriol and stilbestrol, in Clauberg rabbits provided quantitative evidence of the antagonism by estimating carbonic anhydrase activity in the uterine endometrium. This was also associated extremely well with proliferative changes (ratio of glandular to total mucosal area). They suggested thereby the superiority of estimation of uterine carbonic anhydrase as a quantitative test for antiprogestational activity.

The present investigation was made to as-

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