Effect of Environmental Temperature upon Cholesterol Induced Aortic Atherosclerosis in the Rabbit. (25478)

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Hypercholesterolemia and aortic atherosclerosis resulting from cholesterol feeding in rabbits is a well established procedure. Administration of high protein diets(1), alloxan, (2,3), detergents(4), heparin(5), hyaluronidase(6), cholestanol(7), testosterone and estradiol(8), potassium thiocyanate(9), and cortisone(10,11) as well as production of concomitant malnutrition(12), have all been shown to vary the level of blood cholesterol and alter the degree of resulting atherosclerosis in rabbits fed a high cholesterol diet. Similar studies relating degree of hypercholesterolemia and extent of atherosclerosis to age and weight of experimental animals have been reported(13). It is apparent from these studies that degree of hypercholesterolemia is not the sole factor in determining extent of atherosclerotic aortic lesions in the rabbit. Indeed often more marked sclerosis has been demonstrated in those animals with lower serum cholesterol values. A satisfactory explanation of this phenomenon is not apparent. Certainly, the aortic intima varies in its ability to withstand or metabolize plasma lipid loads under varying conditions studied. Seasonal variations in incidence and severity of atherosclerotic complications is a frequently observed clinical phenomenon. Indeed many years ago Mills(14) suggested that variations in climate have a direct effect on death rates from coronary artery disease. Whether environmental temperature itself may induce changes in ability of intimal cells to respond to hypercholesterolemia has not been settled. With this question in mind, we carried out the following experiment using environmental temperature as a variable while attempting to keep other conditions constant. For this experiment we were kindly granted the use of climatic laboratory at the College of Agriculture of Missouri.

Materials and methods. Sixteen 6-month-old, male, albino rabbits were divided into 2 groups. One group was maintained at environmental temperature of 45-50°F, while the other group was kept at 80-85°F. Relative humidity of both groups was maintained at 60-65%. Two rabbits in each group served as controls and ate a measured standard diet of Purina rabbit pellets with water *ad lib.* After 2 weeks, in which food intake and weight gain of both groups were comparable, cholesterol enriched rabbit pellets were substituted in both groups excluding controls. The cholesterol chow was prepared following the method of Wang *et al.*(15). Amorphous pure cholesterol U.S.P. (Merck & Co.) was dissolved in 10% solution of ether and sprayed over thin layers of Purina pellets. After the ether evaporated the cholesterol covered and infiltrated the pellets as a fine film. Average daily intake of cholesterol/rabbit was approximately 1 gram. On the first, 21st, and 42nd day average serum cholesterol levels were determined, following the method of

TABLE I. Average Serum Cholesterol Values for Rabbits Maintained at 45-50°F and 80-85°F.

No. of days fed cholesterol⟶	1st day	21st day	42nd day
Cholesterol fed rabbits at 45-50°F			
Total cholesterol	113.8	1034.1	2073.8
Free "	31.1	372.6	847.8
Esters	82.7	661.5	1226.0
Ester %	72.7	64.0	59.1
Cholesterol fed rabbits at 80-85°F			
Total cholesterol	104.5	1524.8	2632.3
Free "	40.9	672.3	892.8
Esters	63.6	852.5	1739.5
Ester %	60.9	55.9	66.1
Values for rabbits on normal diet after 21 days			
Control rabbits at 45-50°F			
Total cholesterol		102.2	
Free "		22.4	
Esters		79.8	
Ester %		78.0	
Control rabbits at 80-85°F			
Total cholesterol		111.0	
Free "		34.8	
Esters		76.3	
Ester %		69.8	

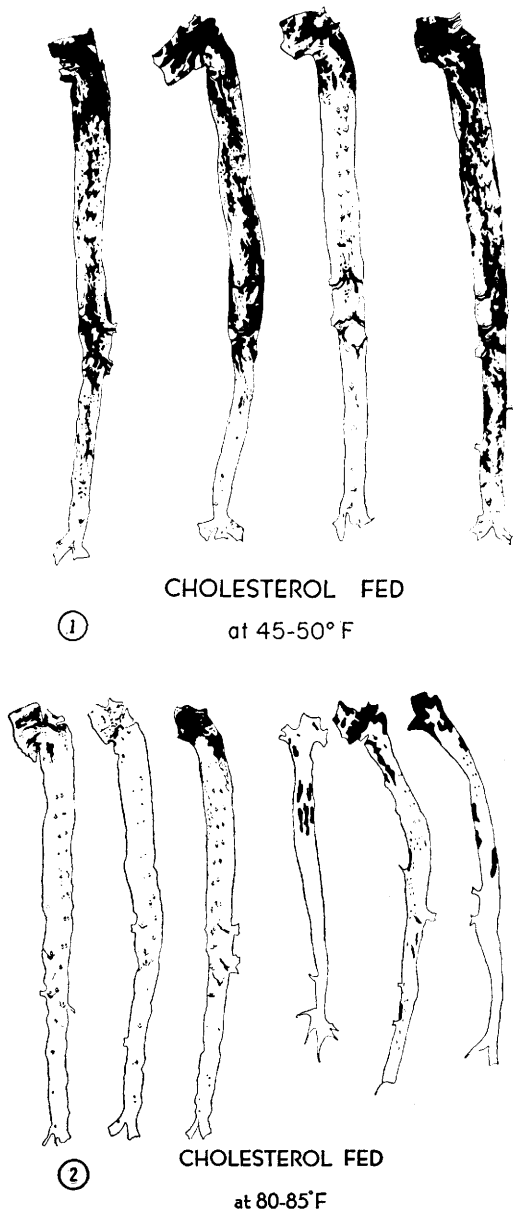

FIG. 1 and 2. Ink drawings showing distribution of aortic sclerotic plaques in rabbits fed cholesterol and maintained at 45-50°F (Fig. 1) and 80-85°F (Fig. 2).

Schoenheimer and Sperry(16) (See Table). On forty-fifth day the animals were sacrificed. Aortas were dissected free of excess fat and fixed in 10% formalin solution for several days, then stained with Sudan IV (usually 2 to 3 minutes), and decolorized with 70% alcohol until good photographic contrast was obtained. From photographs of the mounted aortas, ink drawings were prepared showing distribution of aortic sclerotic plaques. Two rabbits in the 45-50° group and one rabbit in the 80-85° group died shortly after start of experiment and were excluded. One additional rabbit in the 80-85 degree group died following a convulsion on thirtieth day and was included.

Results showed remarkable reduction in plaque formation in animals kept at higher temperature levels in spite of higher total cholesterol and ester values in this group (Fig. 1 and 2). Electrophoretic patterns of sera showed a higher, sharper peak in the beta range in animals kept at higher temperature. Radioactive iodine uptake studies did not reveal any significant difference in the 2 groups.

Summary. The findings indicate that heat stress in rabbits raised under conditions studied, produced a profound effect upon extent and distribution of aortic atherosclerotic plaque formation.

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