Effect of Aortic Constriction on Experimental Atherosclerosis in Rabbits.† (24420)

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Clinical observation has shown that relief of arterial obstruction may be followed by progressive atherosclerosis of the distal arterial tree. Therefore it was decided to ascertain experimentally whether aortic constriction might lessen the production of distal atherosclerosis.

Materials and methods. Thirty adult female rabbits weighing 2-3 kg (5-7 lb) were utilized. Because of relative uninvolvement of the abdominal aorta in experimental atherosclerosis in the rabbit, a bilateral lumbar sympathectomy and periaortic adventitial stripping from renal arteries to aortic bifurcation was carried out in 20 animals. This has been shown by Murphy *et al.*(1) markedly to increase severity of abdominal aortic atherosclerosis in rabbits fed a high cholesterol diet. In 10 of the sympathectomized rabbits a silk ligature was then tied firmly over a No. 6 intestinal needle placed on the aorta at varying levels below the renal arteries. The needle was then withdrawn, leaving an aortic constriction approximately one-third the diameter of the aortic lumen. Ten rabbits served as non-operated controls. All animals were then placed on a pelleted diet as follows: Dehydrated alfalfa meal 96.5%; stabilized animal fat 1.5%; cholesterol U.S.P. .8%; toasted soya flour 1.2%. After 3-month interval, direct pressure tracings were made by introduction of a No. 20 needle into the femoral artery of unanesthetized rabbits and pressures were recorded with pressure transducer and direct writing oscillograph. The animals were sacrificed at 3 months and the entire thoraco-abdominal aorta and iliac arteries were removed. The vessel was opened along its longitudinal axis and fixed in 10% formalin for 24 hours. It was then stained in Scarlet Red solution better to delineate atherosclerotic areas.

Results. Non-operated rabbits. Average femoral artery pressure of these 10 rabbits was 122/94 mm Hg. The animals demonstrated almost solid coalescence of atherosclerotic plaques in the thoracic aorta but only occasional plaques in the lumbar aorta and iliac arteries (Fig. 1a).

Sympathectomized rabbits. Average femoral artery pressure in animals which underwent bilateral lumbar sympathectomy and periaortic adventitial stripping was 124/90 mm Hg. These animals all showed severe involvement of the lumbar aorta and iliac arteries as well as the thoracic aorta (Fig. 1b).

Sympathectomized rabbits with aortic constriction. Average femoral artery pressure in these animals was 84/72 mm Hg. These rabbits demonstrated severe atherosclerosis with coalescence of plaques in the thoracic and lumbar aorta to the level of constriction, but only occasional or rare plaques below that level (Fig. 1c, 1d).

Exposure of abdominal aorta of these animals under ether anesthesia revealed expansile pulsation of the vessel to the level of constriction, but no visible pulsation below that level. Direct pressure measurements above and below the constriction varied considerably because of anesthesia and trauma of the operative procedure, but in all cases demonstrated a marked diminution of pulse pressure below the constriction.

Discussion. In rabbits with sympathectomy and aortic constriction the denervated aorta was subjected to full systolic thrust above the constriction, but this force was considerably damped below that area. Page(2) suggested that atherogenesis is due to accumulation of substances filtered from plasma through the intima by the lateral pressure. Therefore, in this study decreased lateral pressure below the level of aortic constriction may explain diminished atherogenesis as a re-

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FIG. 1. (A) Aorta of non-operated rabbit on high cholesterol diet; (B) aorta of sympathectomized rabbit on high cholesterol diet; (C & D) aortas of sympathectomized rabbits with aortic constriction on high cholesterol diet. (Arrow points to site of constriction.)

sult of decreased filtration of lipemic plasma through the intima.

The mechanism by which sympathectomy increases the severity of abdominal atherosclerosis in rabbits is not clear. Murphy(1) postulated that it is the combination of 2 factors, first, decrease in peripheral resistance and consequent increase in blood flow, and second, weakening of muscular wall of the artery due to paralysis of smooth muscle fibers. It is also possible that the metabolic transport capacity of the normal rabbit lumbar aorta is better able to handle the filtered substances than is the denervated vessel.

Summary and conclusions. Rabbits subjected to bilateral lumbar sympathectomy and fed a high cholesterol diet developed severe atherosclerosis in the lumbar aorta and iliac arteries. When an aortic constriction was concomitantly produced, atherogenesis distal to the constriction was diminished. This was accompanied by a decreased systolic and diastolic pressure, a diminished pulse pressure, and absence of visible aortic pulsation below the constriction.

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2. Page, I. H., *Symposium on Atherosclerosis,* Pub. 338, Nat. Acad. Sci., Nat. Research Council, Washington, D.C., 1954, p5.

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Effect of Bovine Fraction VI on Thyroid Function in the Rat. (24421)

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When normal human serum is labeled with tracer dose of I^{131} thyroxine and electrophoresis carried out on paper strips at pH 8.6 in a barbital buffer $\mu = 0.075$, radioactivity will be located in region of the α-globulins(1), provided the thyroxine level is not too high. Robbins, *et al.*(2) have demonstrated that this is due to the presence at pH 4.5, of a thyroxine-binding protein (TBP) with an isoelectric point close to pH 4. Freinkel, *et al.*(3) have demonstrated the presence of such a TBP in human serum fraction VI but confining their efforts to fraction IV-6 have isolated in very low yields a TBP whose binding capacity appeared to be easily lost(4). We have chosen to work with fraction VI since this fraction, according to the Cohn scheme of fractionation, is richest in glycoprotein.

Method. Bovine fraction VI (BFr VI) isolated according to an extension of Cohn method 10(5) by Pentex Corp. was labeled with I^{131} thyroxine, obtained chromatographically pure from Abbott Laboratories and electrophoresis carried out in duplicate on paper strips under conditions described above. The Spinco Model R paper electrophoresis apparatus was used. In the experiments recorded here, 20 λ of labeled protein solution