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This Week's Citation Classic®

Armstrong M L, Warner E D & Connor W E. Regression of coronary atheromatosis in rhesus monkeys. *Circ. Res.* 27:59-67, 1970.
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Rhesus monkeys developed extensive coronary atherosclerotic lesions in response to an atherogenic diet that was given for 17 months. The lesions decreased markedly after 40 months of corrective diets that were either low in fat or enriched with polyunsaturated fat. [The *SCI*® indicates that this paper has been cited in over 220 publications.]

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This long-term study was done during the latter half of the 1960s. In looking back from our current era of activism in cardiovascular disease, it is amazing to realize how insecure we felt about atherosclerosis. Most physicians regarded human atherosclerosis as an inexorably progressive condition, and increasing evidence to the contrary had not gained sufficient weight to counter widespread defeatism. My colleagues and I also questioned whether the course of atherosclerosis, once established, could be favorably altered. We felt that the best way to test this was by use of controlled observations in an experimental animal model in a species as close to man as possible. Fortunately, trailblazing studies by Bruce Taylor had shown that remarkable lesions could be obtained in Old World Monkeys by a diet enriched in fat and cholesterol.[1] The model of atherosclerosis that we used was the Taylor model. Our contribution consisted in showing that when atherosclerotic monkeys were given therapeutic diets, the atherosclerotic lesions were improved.

I can offer several possible reasons for frequent citation of the paper. One is that it appeared at a time of major shift in the climate of opinion about atherosclerosis. The upbeat implications of our findings fit a changing scene in which large-scale human intervention studies were in the early stages of consideration. Also, the use of a primate model probably lessened the gap that is usually sensed between experimental results and the behavior of human lesions. I also think that our attempts to quantify lesion changes suited a new trend in the research of atherosclerosis in which the presentation of morphometric data became the major thrust of many studies.

Subsequent research has put this paper in the category of background material. More complex studies of regression of experimental atherosclerosis have added much to our knowledge of the limits of regression.[2] Special morphologic features of experimental regression have been noted,[3,4] and, at the University of Iowa, we are studying hemodynamic changes.[5] Even some human lesions are found to regress under precisely observed conditions.[6] Our knowledge of atherosclerosis and its behavior is much greater than it was when the paper appeared, and the possibilities of effective intervention in human atherosclerosis are much clearer.

After this study, William Connor returned to clinical investigation and discovered the important lipid disorder β-sitosterolemia.[7] Emory Warner and I continued working together in experimental atherosclerosis until his death in 1983. Among his awards, Warner was given the Gold-Headed Cane by the American Association of Pathologists in 1981, in part for the research embodied in this paper.

1. **Taylor C B.** Experimentally induced arteriosclerosis in nonhuman primates. (Roberts J C & Straus R, eds.) *Comparative atherosclerosis*. New York: Harper & Row, 1965. p. 215-43. (Cited 35 times.)
2. **Clarkson T B, Bond M G, Bullock B C & Marzetta C A.** A study of atherosclerosis regression in *Macaca mulatta*. IV. Changes in coronary arteries from animals with atherosclerosis induced for 19 months and then regressed for 24 or 48 months at plasma cholesterol concentrations of 300 or 200 mg/dl. *Exp. Mol. Pathol.* 34:345-68, 1981.
3. **Daoud A S, Jarmolych J, Augustyn J, Fritz K E, Singh J K & Kyer T L.** Regression of advanced atherosclerosis in swine. *Arch. Pathol. Lab. Med.* 100:372-9, 1976. (Cited 55 times.)
4. **Wissler R W & Vesselinovitch D.** Studies of regression of advanced atherosclerosis in experimental animals and man. *Ann. NY Acad. Sci.* 275:363-78, 1976.
5. **Armstrong M L, Heistad D D, Marcus M L, Piegors D J & Abboud F M.** Hemodynamic sequelae of regression of experimental atherosclerosis. *J. Clin. Invest.* 71:104-13, 1983.
6. **Blankenhorn D A.** Progression and regression of femoral atherosclerosis in man. *Atheroscler. Rev.* 3:169-82, 1978.
7. **Bhattacharyya A K & Connor W E.** β-sitosterolemia and xanthomatosis: a newly described lipid storage disease in two sisters. *J. Clin. Invest.* 53:1033-43, 1974. (Cited 65 times.)

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