COMMENT

The literature on experimental arteriosclerosis is replete with statements that atherosclerosis cannot be induced in omnivores or carnivores by cholesterol feeding and that cholesterol causes lesions in the herbivorous rabbit (and guinea pig) because it is foreign to the rabbit's usual metabolism. Our earlier experiments clearly showed that feeding cholesterol in cottonseed oil will cause atheroma in the omnivorous chick and that the blood cholesterol of an omnivore can be elevated by cholesterol feeding. Our present results show more specifically that cholesterol itself, and not cottonseed oil or underfeeding, is responsible for the production of vascular lesions in the chick. Furthermore, not only do simple atheroma be thus induced, but also all the stages of the lesions commonly designated as arteriosclerosis, namely, intimal lipoidosis, fibrosis, hyalinization, calcification, ulceration, and aneurysm formation. In the light of our results it seems that too much emphasis has been placed on the herbivorous character of the rabbit in evaluating the rabbit experiments.

While cottonseed oil feeding and underfeeding may be contributing factors in the development of arteriosclerosis, cottonseed oil feeding alone in the chick as in the rabbit does not result in vascular lesions. Similarly, generalized undernutrition through underfeeding of a balanced mash, without any specific deficiencies, will not of itself cause atherosclerosis, although undernutrition has been related both to the development of fatty liver and the elevation of blood cholesterol. Spontaneous arteriosclerosis has a clearer higher incidence in male than in female chicks, but the lesions' underdevelopment occurring in cholesterol-fed chickens did not prevent arteriosclerosis. Apparently, therefore, absence of the hormones elaborated by the mature testis does not interfere with the arteriosclerosis induced by cholesterol feeding. Our experiments, however, do not reveal whether or not the administration of estrogens to these eunuchoid cocks would have an inhibitory effect on the vascular lesions. Experiments on rabbits indicate that both estrogens and androgens prevent cholesterol arteriosclerosis in females but not in males.

An objection frequently raised to the experiments on rabbits is that the lesions caused by cholesterol feeding, while they resemble those of man, are totally unlike the vascular changes occurring spontaneously in rabbits. In chicks as in rabbits the human arterial lesions have been clearly reproduced. But unlike the cholesterol-induced lesions in rabbits, those in chicks do resemble the spontaneous lesions. Fox described the characteristic spontaneous arteriosclerosis of both sexes consisting of areas and streaks of yellow atheromatous material, most prominent in the sinus of Valsalva and the arch of the aorta. He found thinning and distortion of vessel walls with narrowing of the lumina to slitlike apertures. In thin-walled vessels the yellow deposits may be visible externally. This description is so applicable that it might have been written for the lesions induced by cholesterol in our chicks. Fox found such atherosclerotic deposits in 3 of 100 ground fowl averaging 3 years of age. From our observation and that of others, there is another spontaneous lesion. It is intimal fibrosis, and it occurs in much higher incidence in the muscular arteries of younger cockerels (26 of 32). While it may contain lipoid, it is clearly different from the lesion described by Fox. We must conclude that there are two distinct lesions.

24. (a) Keslen and others. (b) Uchiyama. (c) Fox.
Classic Pages

Circ Res. 1970;27:212
doi: 10.1161/01.RES.27.2.212

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1970 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/27/2/212.citation