REGRESSION OF EXPERIMENTAL ATHEROSCLEROSIS OF THE AORTA IN GUINEA PIGS

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UDC 616.132-004.6-092.9-003.95

Resorption of lipids from atherosclerotic plaques on the aorta in guinea pigs developing after discontinuing an atherogenic diet takes place slowly and unevenly and is accompanied by qualitative changes in the lipids. Disintegration of lipid macrophages takes place at the same time, and in the late period of the investigation they disappear completely from the plaques. Remnants of disintegrating masses of lipids, cholesterol crystals, and deposits of lime remain behind in the pathological foci until the latest stages of resolution. Complete removal of all lipids is rarely observed. Removal of lipids takes place mainly through elution by a current of lymph. Resorption of lipids by cells is less important.

Regression of experimental atherosclerosis has now been reproduced in many species of laboratory animals (rabbits [2,7,8,12], dogs [6], rats [11], and birds [9]). The only exception to this has been guinea pigs, in which the only published researches have been concerned with the progression of atherosclerosis, [1,3-5,10].

The object of this investigation was to study the consecutive stages of regression of experimental atherosclerosis in the aorta of guinea pigs. Experiments were carried out on 54 male guinea pigs weighing 150-300 g.

EXPERIMENTAL METHOD AND RESULTS

Macroscopic changes were found in the aorta only after feeding with cholesterol for 3 months (half an egg yolk daily). The initial atherosclerotic changes consisted of deposition of a very small amount of diffuse and finely particulate lipids between the endothelium and the internal elastic membrane. As the duration of the experiment increased (from the 4th to the 6th month), the quantity of lipids in the subendothelial layer gradually increased. Among the diffuse and finely particulate lipids, a few large drops began to appear in the foci of fatty infiltration, together with solitary cells, mainly lipid macrophages (Fig. 1a). Lipids were also found in small amounts in the somewhat widened spaces between the elastic membranes of the inner layers of the tunica media.

Fibrous structures were extremely feebly developed. Hyperplasia of the internal elastic membrane was observed (Fig. 1b). The number of argyrophilic fibers was slightly increased.

Fully formed plaques were visible in the aortas of guinea pigs sacrificed at the longest period after the beginning of feeding with egg yolks (9 months).

In the early stages after discontinuation of cholesterol feeding (1-3 months), the atherosclerotic changes in the aorta were essentially indistinguishable from those observed at the height of feeding. During these periods, not only did the lipid content in the plaques not diminish, but it actually increased slightly both through the greater accumulation of extracellular lipids, diffusely infiltrating the ground substance of the plaque, and also through an increase in the quantity of lipids present in the cytoplasm of the lipid macrophages. In many macrophages, signs of degeneration and disintegration were found.

At the 6th month of regression, some degree of irregularity was observed in the distribution of lipids in a few of the plaques, caused by the appearance of areas of interstitial substance almost free from lipids (Fig. 2a). Among the extracellular lipids, an increase was also found in the size of the granular masses

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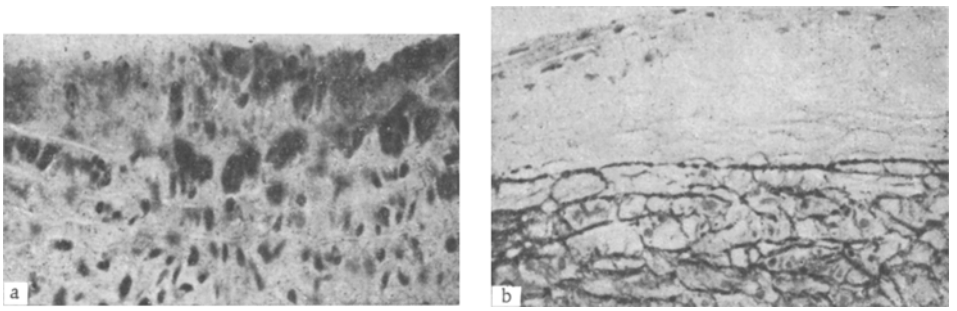

Fig. 1. Dynamics of atherosclerotic changes in aorta of guinea pigs. a) Uniform infiltration with diffuse lipids into interstitial substance of intima of aorta (3 months on atherogenic diet). Sudan III – hematoxylin, 390 . b) Feeble development of elastic fibers in plaque (9 months of cholesterol feeding). Weigert–Hart, 476 ×.

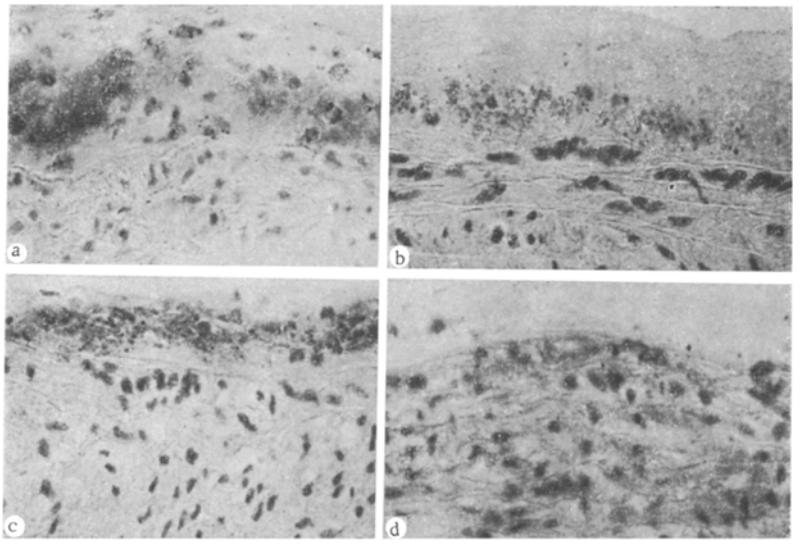

Fig. 2. Dynamics of regression of atherosclerotic changes in the aorta of guinea pigs. a) Irregular distribution of lipids in an atherosclerotic plaque (6 months of regression), Sudan III – hematoxylin, 240 ×; b) coarsely granular lipids, cholesterol crystals, and granules of lime visible in an atherosclerotic plaque (6 months of regression), Sudan III – hematoxylin, 240 ×; c) remnants of lipid granules in deep layers of plaque at border with internal elastic membrane (12 months of regression), Sudan III – hematoxylin, 240 ×; d) total absence of lipids in a small atherosclerotic plaque (15 months of regression), Sudan III – hematoxylin, 476 ×.

with cholesterol crystals and deposition of lime (Fig. 2b). The fibrous framework of the plaques, argyrophilic fibers, and elastic fibrils were found mainly where cells were accumulated.

From the 6th to the 10th month of regression, concurrently with a reduction in the quantity of lipids in the plaques, the formation of new argyrophilic fibers continued and they underwent conversion into collagen fibers.

In the later stages (12–18 months), the atherosclerotic plaques in the aorta contained very little lipoid material, located mainly in the deep layers of the intima along the internal elastic membrane (Fig. 2c). The lipids consisted of granular masses, among which were cholesterol crystals and sometimes considerable deposits of lime. Compared with the preceding periods, the plaques were slightly flatter (Fig. 2d).

The development of atherosclerotic changes in the aorta in guinea pigs starts with deposition of diffuse and finely particulate lipids in the subendothelial layer. With an increase in the quantity of lipids in the pathological foci, reactive hyperplastic changes take place in the cellular and, to a lesser degree, the fibrous structures of the arterial wall. After feeding on a cholesterol-rich diet is discontinued, resorption of lipids takes place slowly and irregularly from the plaques. During regression, the finely particulate lipids are gradually converted into coarsely granular, disintegrating masses, among which cholesterol crystals are deposited and calcium soaps are formed. Meanwhile the lipid macrophages break up. Complete disappearance of lipids is rarely seen. Removal of the lipids takes place mainly through their gradual transfer outward into the tunica media.

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