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Are Foamy Cells in Atheromata of Reticulo-endothelial Origin? (19410)

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Although plausible reasons have been advanced for believing that cholesterol esters are carried into the atherosclerotic vessel wall by macrophages(1-3), more recent studies support another view. Kuntz and Sulkin(4) concluded that foam cells of atheromata arose *in situ* from vascular endothelium, and in rabbits with early atherosclerosis given India ink or lithium carmine intravenously thrice at 2-day intervals they observed pigment granules in foam cells in the liver and spleen, but not in atheromata. The interval between the last injection and death of the animals was not stated, but presumably was short. Duff and McMillan(5) gave Thorotrast to atherosclerotic rabbits at intervals of 5 minutes to 4 days before death. Thorotrast was found in foam cells in the superficial part of the plaques and in some endothelial cells overlying the plaques. Simonton and Gofman(6) administered Thorotrast to rabbits, and subsequently began cholesterol feeding. Thorium-containing phagocytes in the liver and spleen engulfed India ink injected 24 hours before death. Radioactivity in atheromata was low, and the authors concluded that macrophage migration was not a significant source of foam cells of atheromata.

In view of the brevity of the interval between labeling of the reticulo-endothelial cells and death in the experiments cited, and since thorium-laden cells may perhaps migrate less readily than others, our experiments may be of interest.

Methods. Atherosclerosis was induced by incorporation in the diet of young adult rabbits of 3% of a 10% suspension of cholesterol in cottonseed oil. After 2 weeks, weekly intravenous injection of 3 cc of 17% Higgins India ink in normal NaCl solution was instituted. The duration of cholesterol administration was as follows: one rabbit, 3 months; 4 rabbits, 6 months; and one rabbit, 10 months. Two control rabbits were given ink for 10 months.

Results and discussion. There was a small intimal plaque in the ascending aorta of each control rabbit. The aorta of the rabbit that received cholesterol for 3 months was normal. The remaining animals had severe atherosclerosis. The reticulo-endothelial cells of all rabbits were laden with carbon. Although cells with foamy cytoplasm were abundant in the atheromata, no carbon-containing phagocytes were present. Absence of pigmented phagocytes from the aorta of the controls should be expected, since Leary(1) stated that macrophages in man and in experimental animals in which a great variety of forms of particulate matter have been engulfed exhibit no tendency to invade arterial walls.

While few animals were used, it was obvious that use of larger numbers would be futile. The results are more in accord with the view that cholesterol esters enter blood vessel walls by diffusion than with that that they are transported therein within migrating reticulo-endothelial cells.

Summary. Atherosclerosis was induced in rabbits by administration of cholesterol while the reticulo-endothelial cells were being laden

with carbon. Carbon-laden phagocytes were not found in the atheromata.

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Comparative Blood Volume Changes in Anti-Platelet Serum Shock and Other Types of Shock.* (19411)

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Haematological changes observed(1) in anti-platelet serum shock, have indicated that haemodilution occurred in this type of shock. It seemed desirable, therefore, to study changes in the absolute volumes of red cells and plasma, respectively. Studies are presented in this paper which show results in anti-platelet serum, histamine, trypsin and peptone shock.

Methods. All experiments were done with dogs. Plasma volumes were determined by the injection of Evans blue dye (T-1824). Since radioactive substances were not available, another method was employed(2) for the determination of total cell volume, using red blood cells with methaemoglobin. The amount of anti-platelet serum injected for inducing shock varied with the titer of the serum.

Results. Table I shows plasma, red blood cell, and total blood volume determinations in different types of shock. In all observations the total blood volume diminished in anti-platelet serum shock. Identical results were observed in histamine shock. These results are in agreement with those of other authors who have studied histamine and other types of shock. Increase of total blood volume was observed in 2 dogs shocked by trypsin; the significance of these data requires further study.

Plasma volume diminished in all the animals, except those shocked by trypsin, in which it increased. The total red cell volume increased in both animals with tryptic shock, in one case of anti-platelet serum shock and in one of histamine shock. In all other observations (11 out of 16) the total red cell volume diminished (Table II). The ratio between the decreases of plasma and red cell volumes varied according to the type of shock. In anti-platelet serum shock the red cell volume decreased more than the plasma volume. This occurred occasionally in histamine shock also, but generally the reverse was observed, *i.e.*, a more accentuated decrease of the plasma than the red cell volume.

When methaemoglobin-labeled red cells were injected after shock had been induced, a greater proportion of methaemoglobin remained in the circulation than when a comparable amount of labeled cells were injected in normal animals (Table III). Since the number of labeled cells given before and after shock was not identical, a correction was used assuming that there was a linear relationship between the amount of methaemoglobin administered and that found in the peripheral blood. That such an assumption is valid is shown by the following experiment performed 3 times on the same dog:

Day of exp.	MetHb inj.	Circulating MetHb/100 g Hb
1	1.5	3.6
2	2.5	5.2
3	5.2	10.3

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