EFFECT OF COOLING ON DEVELOPMENT OF EXPERIMENTAL LIPOIDOSIS OF THE CORONARY ARTERIES

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The effect of repeated cooling on the development of atherosclerosis in general and atherosclerosis of the coronary arteries in particular has been inadequately studied. The clinical and pathological data available on this subject are few in number and contradictory in nature [1-4, 6, 11].

Very little attention has been paid to the problem of changes in lipid metabolism in the experimental studies which have been made of adaptation of the organism to cold climatic conditions [7, 8, 12, 13]. Only a few isolated investigations have been made of the changes in the energy balance of the organism and in lipid metabolism in the course of adaptation to cold [5, 16].

The object of the present investigation was to study the development of lipoidosis of the coronary arteries in albino rats under the influence of repeated exposure to cold.

The animals of this species are known to possess high resistance to the development of vascular lipoidosis, which cannot be produced in them solely by a high alimentary intake of fat and cholesterol [10, 14, 15]. It was, therefore, interesting to determine whether lipoidosis of the coronary arteries would develop in rats as a result of combined alimentary cholesterol loading and repeated cold stress.

EXPERIMENTAL METHOD

Experiments were conducted on 35 male albino rats with an initial weight of about 250 g.

To reproduce cold stress the experimental animals were placed for 1 h daily in a cold chamber at a temperature of between — 20 and — 22°. The rats were kept in glass jars covered with wire gauze which restricted their movement and prevented them from warming one another. Besides this, the experimental animals each received 4 ml of a 10% solution of cholesterol in sunflower oil by intragastric injection from a syringe fitted with an olive. The control rats received cholesterol in oil daily without cooling.

The animals were sacrificed by decapitation after 8 (series I), 20 (series II), and 10 days (series III), of the experiment. For the histological investigation the heart was cut transversely into three approximately equal parts. Serial sections were cut to a thickness of about 15 μ from the cranial part of the base of the heart, where the initial branches of the coronary arteries are located. From the middle and caudal parts of the heart every 15th section was investigated. Usually vessels affected by lipoidosis were found in the cranial third of the heart — mainly arteries branching from the aorta and their branches of the first and second order.

EXPERIMENTAL RESULTS

Lipoidosis of the branches of the coronary arteries was found in all 3 experimental rats of series I, but was completely absent in the two control animals. The lesions of the coronary arteries in the experimental animals had the appearance of small foci in the intima of the large branches or of bands parallel to the lumen in the media of the vessel (Fig. 1). Vessels affected by lipoidosis were found in $\frac{1}{3}$ of the sections from each experimental animal. In one case, examination of serial sections showed a focus of lipoidosis crossing from the intima into the media and then spreading out like a fountain in the adventitia.

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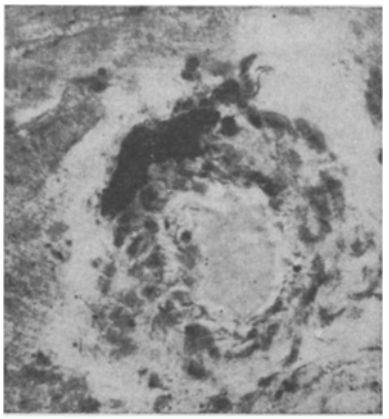

Fig. 1. Development of segmental lipoidosis of the media in a branch of the coronary artery. Day 8 of the experiment. Sudan IV. Objective 20×, ocular 7×.

These pictures evidently reflect to some extent the reversibility of the process, demonstrating how lipids may pass through the whole thickness of the vessel wall. In this connection, it is interesting to note that the distribution of lipids in the media and adventitia of the arteries in rats and dogs with lipoidosis may be associated with the fact that in animals of these species the blood lipoproteins consist mainly of particles of small size [17], so that if their breakdown in the vessel wall is disturbed they may not only be retained in the intima, but they may also penetrate deeper.

Of the 14 animals sacrificed on the 20th day of the experiment (series II) all 6 control rats and also 7 of the 8 experimental animals were free from lipoidosis of the coronary arteries. In 1 experimental rat, however, a very widespread coronary lipoidosis was found, affecting branches of the coronary arteries in nearly every section of the cranial third of the heart.

Lipids were distributed as small, irregular foci (Fig. 2) in the intima (two or three foci can be seen in a section through one vessel, usually on opposite sides) and also as bands in the media. In one case a circular lesion of the media was observed in a branch of the coronary artery. The lesions were seen mainly in branches of the coronary arteries of the first and second, and more rarely, the third orders. Lipoidosis was never accompanied by the development of sclerosis of the vessels or by the formation of xanthoma cells.

Because coronary lipoidosis was seen in this experimental material more often in the short (8 days) than in the long (20 days) experiments it was decided to verify the data relating to the role of repeated cooling in experiments of short duration. Accordingly, the experiments of series III were carried out on 16 albino rats, of which 7 were experimental and 9 control. As stated above, the animals were sacrificed after 9 or 10 daily exposures to cold accompanied by alimentary loading with fat and cholesterol (experiment), or after "pure" fat and cholesterol loading (control). The results of this series of experiments also conformed the possibility of development of lipoidosis of the coronary arteries under the influence of repeated cooling combined with feeding with fat and cholesterol. Among the experimental rats lipoidosis of the branches of the coronary arteries (indistinguishable in its morphological manifestations from that observed in the animals in the series I experiments) was found in 4 rats, but was absent from all 9 control rats.

Hence, some animals exposed to repeated cooling combined with alimentary loading with fat and cholesterol developed lipoidosis of the coronary arteries. Interest in these results is heightened by the fact that they were not obtained in herbivorous animals (rabbits, for example, in which arterial lipoidosis may be reproduced readily by the alimentary route, but in omnivorous animals (albino rats), known to possess marked resistance to alimentary lipoidosis.

Lipoidosis of the coronary arteries arising in rats under the influence of cooling and alimentary loading with fat and cholesterol is evidently a reversible process, as is illustrated by certain morphological findings and also by the lower frequency of involvement of the arteries in the later period of the experiment

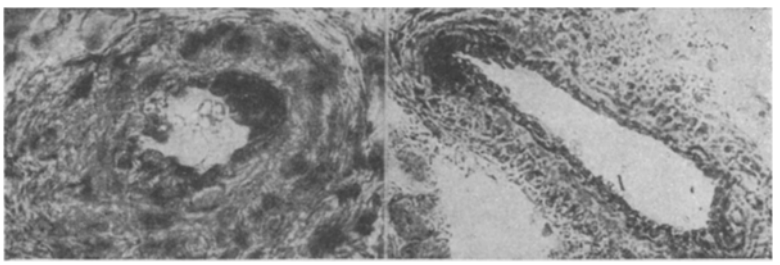

Fig. 2. Lipoidosis of the intima of branches of the coronary arteries in an animal sacrificed after 20 days of the experiment. Sudan IV. Objective 40×, ocular 7×.

than in the earlier period. Perhaps the lipids deposited in the walls of the arteries may gradually be absorbed and carried away by the lymphatics in the process of physiological adaptation to cold. It is interesting to note, however, that if lipoidosis was found in the later period of the experiment (as was the case in one of the animals sacrificed after 20 days), it was unusually severe and extensive. This suggests that in certain animals, on account of a disturbance of the mechanism of adaptation to cold, the phenomena of lipoidosis of the coronary arteries may persist or even become intensified. If these observations are confirmed by future studies, this will justify the conclusion that a similar mechanism is concerned with the development of coronary lipoidosis in Arctic conditions among those persons who have difficulty in adapting themselves to cold.

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