CONTRACTILE PROPERTIES OF SMOOTH-MUSCLE CELLS OF THE AORTA DURING THE DEVELOPMENT OF EXPERIMENTAL ATHEROSCLEROSIS

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Contractile responses of smooth-muscle cells to the action of catecholamines and KCl at 27 and 37°C, under normal conditions and in the initial stages of atherosclerosis, were investigated in experiments on isolated ring segments of the rabbit aorta. The contractile responses of the atherosclerotic aorta induced by KCl were of lower amplitude than in the intact aorta, but the opposite pattern was found after the action of catecholamines. Lowering the temperature depresses the contractile responses of both the normal and the atherosclerotic aorta.

KEY WORDS: aorta; atherosclerosis; contractility.

Atherosclerosis may involve not only the intima, but also the media of blood vessels [1]. Accumulation of lipids in the media is observed less commonly than in the intima [4], but processes of lipid infiltration spread more rapidly to the affected portions of the media of the aortic wall [10]. Disturbance of the function of cells in the media of the aorta facilitates progression of the atherosclerotic process [13]. Even in the

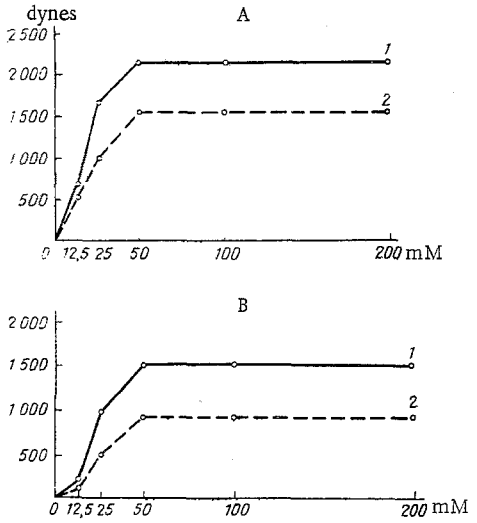

Fig. 1. Dose-response curves for different KCl concentrations: A) 37°C; B) 27°C. 1) Intact aorta; 2) atherosclerotic aorta. Ordinate, contractile activity of aorta (in dynes); abscissa, KCl concentrations (in mM).

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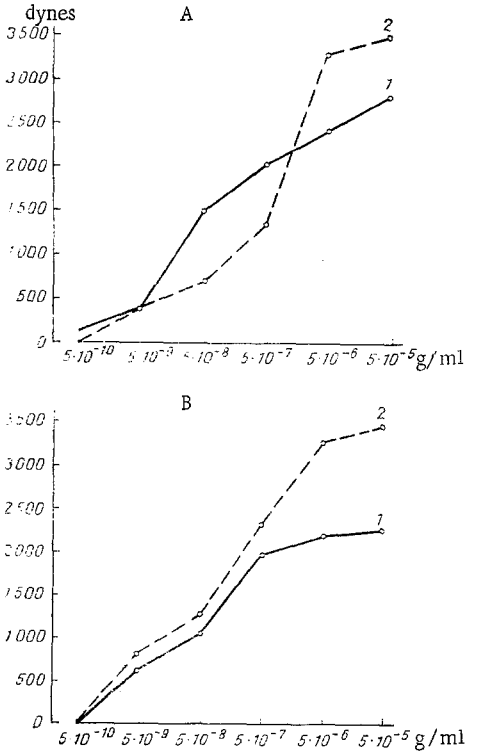

Fig. 2. Dose-response curves for increasing concentrations of NA. Abscissa, NA concentration (in g/ml). Remainder of legend as in Fig. 1.

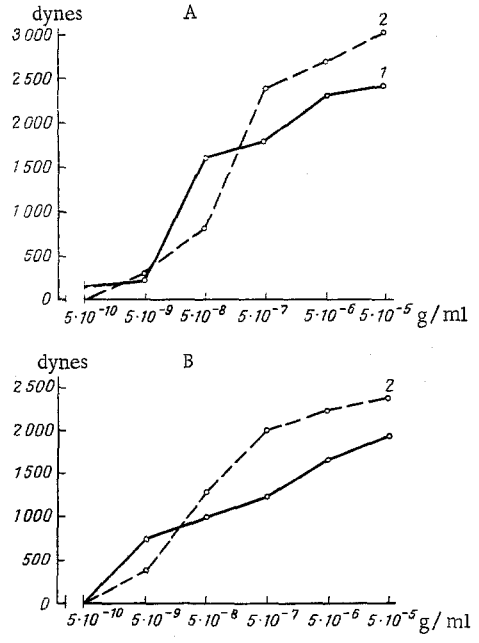

Fig. 3. Dose-response curves for increasing concentrations of A. Abscissa, concentration of A (in g/ml). Remainder of legend as in Fig. 1.

early stages of atherosclerosis the accumulation of mucopolysaccharides, glycogen, and ascorbic acid is observed in the smooth-muscle cells [2, 5], but the contractile power of the smooth muscle cells of the blood vessels in atherosclerosis has not been studied.

The contractile activity of the aorta of rabbits with experimental atherosclerosis was investigated.

EXPERIMENTAL METHOD

Isolated ring segments of the thoracic aorta of normal rabbits and rabbits with experimental atherosclerosis were used [3]. Cholesterol was given to the rabbits with the diet in a dose of 1 g daily for 6 weeks. Immediately after sacrifice of the animals (air embolism) the aorta was removed and kept in Krebs' solution. The preparations were kept for not more than 24 h at 4°C until the time of the experiments. Ring segments of the aorta, 1 mm wide, were placed in a transparent plastic constant-temperature chamber with a capacity of 6 cm^3 containing running oxygenated Krebs' solution of the following composition (in mM): NaCl 120.4, KCl 5.9, $NaHCO_3$ 15.5, $MgCl_2$ 1.2, NaH_2PO_4 1.2, $CaCl_2$ 2.5, and $C_6H_{12}O_6$ 11.5. The ring segments were fitted on the liver of a mechanotron and on a stationary fixing device and stretched with a force of 2 g. The preparations were kept in the chamber for 2 h before the beginning of the experiment with this degree of initial stretching. To record the contractile activity of the intact and atherosclerotic aorta simultaneously and under identical conditions, two similar 6MKhIS mechanicoelectrical transducers, set up in parallel were used. Noradrenalin bitartrate (NA) and adrenalin hydrochloride (A) were added to the Krebs' solution in concentrations of between $5 \cdot 10^{-10}$ and $5 \cdot 10^{-5}$ g/ml. In some experiments KCl in concentrations of 12.5, 25, 50, 100, and 200 mM was added consecutively to the Krebs' solution. The pH of the solution was 7.2-7.4.

Altogether 398 measurements were made on 64 preparations. Statistical analysis of the results was carried out with the aid of the nonparametric Wilcoxon–Mann–Whitney criterion.

EXPERIMENTAL RESULTS AND DISCUSSION

The addition of KCl or catecholamines to the Krebs' solution (at 27 or 37°C) caused a distinct contractile effect of both the control and the atherosclerotic aorta.

Dose-response curves for the action of KCl are shown in Fig. 1. A threshold KCl concentration of 12.5 mM and a concentration evoking maximal contraction of 50 mM were common to both preparations. Meanwhile the absolute values of the contractile response of the intact aorta were higher than those of the atherosclerotic aorta ($P < 0.001$). Reducing the temperature of the solution by 10°C clearly ($P < 0.001$) reduced the amplitude of the contractile responses but the ratio between the responses of the intact and atherosclerotic preparations remained the same. At both temperatures, with an increase in the KCl concentration the latent period of the responses and the time taken to reach the maximum of contraction were reduced, whereas the period of relaxation was lengthened. At the lower temperature the temporal parameters of the contractile responses were lengthened for both preparations.

Contractile responses of the aortic rings were different in the presence of catecholamines (Figs. 2 and 3). The first feature to be noted in this case is the greater ($P < 0.001$) amplitude of the contractile responses of the atherosclerotic aorta. Meanwhile the parallel dynamics of the dose-response curves of the intact and atherosclerotic preparations that were found with KCl were absent in this case. At 37°C the threshold catecholamine concentration for the atherosclerotic aorta was increased; a further increase in concentration caused an increase in amplitude of the contractile responses and, finally, at certain concentrations ($5 \cdot 10^{-7}$ g/ml for NA and $5 \cdot 10^{-6}$ g/ml for A) the contractile response of the atherosclerotic aorta exceeded that of the intact aorta. Lowering the temperature to 27°C had two effects: It equalized the threshold concentrations of cathecholamines and it increased the excess of contractile responses of the atherosclerotic preparations over the intact. This last effect was more pronounced in the case of A.

One of the main changes in the media of the aorta in the early stages of atherosclerosis is an increase in the content of acid mucopolysaccharides and in the accumulation of lipids [4, 7]. The greater amplitude of the contractile responses to catecholamines in the atherosclerotic aorta can be explained by the ability of mucopolysaccharides to bind Na^+ [12].

For many reasons a shift of the Na^+ membrane gradient can give rise to changes in the contractile responses of smooth-muscle cells [6, 8, 10, 11, 15].

The decrease in amplitude of the contractile responses in a solution at lower temperature is evidently due to depression of the ionic permeability of the membrane and lowering of ATPase activity. Contractions of the preparations at the lower temperature also could be superposed on an increase in their tone, for under those circumstances the activity of the sarcoplasmic calcium pump is inhibited [9].

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BILE SECRETORY FUNCTION OF THE LIVER IN BIRDS OF DIFFERENT AGES WITH EXPERIMENTAL ATHEROSCLEROSIS

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The bile-secretory function of the liver under normal conditions and in experimental atherosclerosis produced by administration of cholesterol was studied in experiments on young (3-4 months old) and adult (30-36 months old) hens of the Russian White breed. During natural aging a decrease in the total and free cholesterol concentrations in the blood serum and in the bile-secretory function of the liver was observed. These indices were raised during administration of cholesterol and atherosclerotic changes developed in the aorta. The severity of these changes compared with normal was greater in the adult than in the young experimental birds.

KEY WORDS: experimental atherosclerosis; age; bile acids; cholesterol; liver.

Disturbances of the metabolism, structure, and function of the liver play an important role in the pathogenesis of atherosclerosis [2, 8, 11].

Changes in the bile-secretory function of the liver were studied in birds of different ages under normal conditions and with experimental atherosclerosis caused by chronic cholesterol loading.

EXPERIMENTAL METHOD

Experiments were carried out in the fall and winter on hens of the Russian White breed of two ages: 3-4 months (the hens begin to lay at the age of 5-6 months) and 30-36 months (laying, which had ceased because of

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