ANALYSIS OF ELECTRICAL ACTIVITY IN THE BLOOD VESSEL WALL IN EXPERIMENTAL ATHEROSCLEROSIS

A. K. Chepurov

UDC 616.13-004.6-092.9-073.97

Electrical activity of the walls of intact blood vessels and the blood vessels of rabbits kept on an atherogenic diet was investigated in a transparent plastic chamber containing aerated Krebs' solution. With the development of atherosclerotic changes in the vessel wall, the potential difference between its intima and adventitia is reduced. The most marked morphological and electrical changes in the vessel wall in atherosclerosis are observed in the abdominal aorta and femoral artery.

Clinical and experimental investigations have shown that atherosclerosis is manifested principally by morphological and functional changes in the blood vessel wall [1, 2, 5, 7, 8, 11, 16]. The coagulant activity of the vessel wall is increased and its anticoagulant and fibrolytic activity is reduced [6, 12, 14, 15]. It is considered that changes in the coagulant properties of the vessel wall and disturbance of its morphological integrity are important factors in the pathogenesis of intravascular thrombosis in atherosclerosis [6, 10, 15]. Most workers state that functional changes in the vessel wall in atherosclerosis are associated with metabolic disturbances taking place in it [11, 16]. Recent work has shown that active ion transport takes place through the vessel wall, and is determined by the character of its electrical activity and the magnitude of the zeta-potential of the boundary layer of moving blood [3, 4, 9, 16]. It can therefore be postulated that atherosclerosis is accompanied by changes in the electrochemical characteristics of the vessel wall.

The object of the present investigation was to study the electrical activity of the intact vascular wall and its changes in the wall of blood vessels of rabbits with experimental atherosclerosis.

EXPERIMENTAL METHOD

Experiments were carried out on 17 rabbits weighing 2.5-3 kg. Group 1 consisted of control animals (9 rabbits), group 2 of animals receiving cholesterol in a dose of 0.5 g/kg body weight daily with the diet for 8 months (8 rabbits). The most marked changes in atherosclerosis are observed in the femoral vessels, at the bifurcation of the aorta, and in the abdominal aorta. Accordingly, electrical activity was studied in the abdominal parts of the aorta and inferior vena cava, and also in the femoral artery and vein. For this purpose, the blood vessel to be investigated was excised under intravenous urethane anesthesia (10 ml of a 20% solution) and all the perivascular tissues carefully removed. The dissected part of the blood vessel, 4-5 cm long, was incised longitudinally. The apparatus used to study electrical activity of the vessel wall in vitro is shown diagrammatically in Fig. 1. The segment of blood vessel for testing was placed between two halves of a transparent plastic chamber, joined together hermetically by means of screws. The two halves of the chamber were filled with Krebs' solution of the following composition (in g/liter): NaCl 7.7; $NaHCO_3$ 1.36; NaH_2PO_4 0.165; KCl 0.347; $CaCl_2 \cdot 6H_2O$ 0.272; $MgCl_2 \cdot 6H_2O$ 0.01; glucose 1.4. The Krebs' solution was titrated to pH 7.4. Agar bridge electrodes, prepared in the usual way, were placed 2 mm away from the surface of the intima and adventitia of the blood vessel. The other ends of the agar bridge elec-

Research Institute of Age Physiology, Academy of Pedagogic Sciences of the USSR, Moscow. (Presented by Academician V. V. Parin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 71, No. 5, pp. 31-34, May, 1971. Original article submitted June 25, 1970.

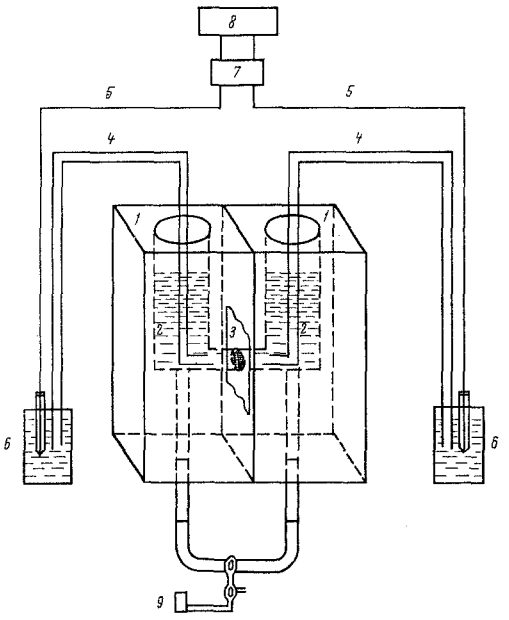

Fig. 1

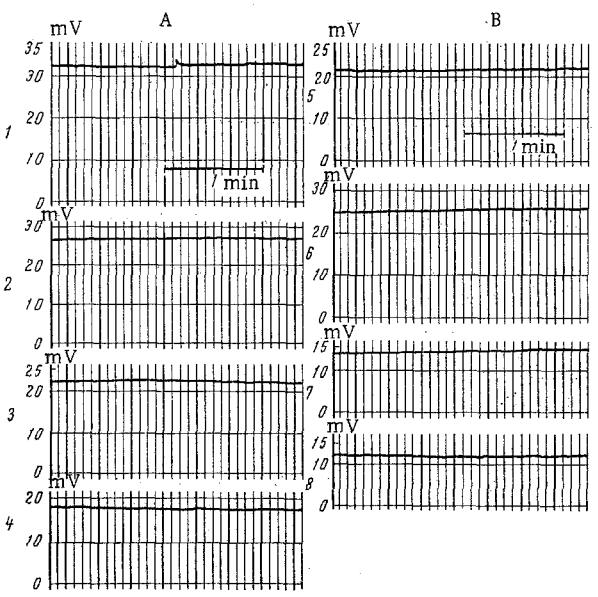

Fig. 2

Fig. 1. Diagram of apparatus for measuring electrical activity of blood vessel wall in vitro: 1) separate half of transparent plastic chamber; 2) Krebs' solution; 3) tissue of blood vessel to be tested; 4) agar bridge electrodes; 5) calomel electrodes; 6) jars containing 2.7 M potassium chloride solution; 7) LPU-01 pH-meter; 8) KSP-04 potentiometer; 9) system for aerating Krebs' solution.

Fig. 2. Electrical activity of intact blood vessel wall (A) and vessel wall of rabbits with experimental atherosclerosis (B): 1 and 5) abdominal aorta; 2 and 6) abdominal portion of inferior vena cava; 3 and 7) femoral artery; 4 and 8) femoral vein.

trodes were placed in jars containing 2.7 M potassium chloride. Calomel electrodes were inserted into the same jars and made contact with wires connecting them to the input of a type LPU-01 pH-meter. The potential difference between the intima and adventitia of the blood vessel was recorded graphically by means of a type KSP-04 automatic electronic potentiometer. Calibration of the recorded potential difference and determination of its polarity were carried out by a type I-01 electrode system simulator. The potential difference between the agar bridge electrodes placed in Krebs' solution was 1.5-2 mV, and the drift of the amplifier system while recording electrical activity in the vessel wall was virtually zero.

In the course of the investigation the blood cholesterol of intact rabbits and of rabbits kept on an atherogenic diet was determined and a morphological control was provided.

EXPERIMENTAL RESULTS AND DISCUSSION

The potential difference between the intima and adventitia of the blood vessel was stable in character (Fig. 2). The intima was charged negatively relative to the adventitia of the blood vessel. Comparative analysis of the potential difference of the blood vessels investigated showed marked differences between them (Fig. 2A). For example, the greatest potential difference (32.5 ± 1.6 mV) was recorded in the abdominal aorta. The potential difference between the intima and adventitia of the inferior vena cava, femoral artery, and femoral vein was 26.6 ± 1, 22.5 ± 2, and 18 ± 1.7 mV ($P < 0.05$).

A study of the potential difference between the intima and adventitia of the blood vessels of rabbits kept on an atherogenic diet revealed significant differences from the controls (Fig. 2B). The potential difference of the abdominal aorta of rabbits with atherosclerosis was reduced by 10.8 ± 1.5 mV ($P < 0.02$) compared with the intact abdominal aorta. The potential difference of the wall of the inferior vena cava in rabbits receiving cholesterol was only 3.6 ± 1 mV below that of the intact inferior vena cava ($P < 0.05$). The potential difference between the intima and adventitia in the femoral artery of rabbits with experimental atherosclerosis was 8.4 ± 2.3 mV ($P < 0.01$) below that of the femoral artery of the control animals. The

potential difference of the femoral vein in rabbits with atherosclerosis was 5.6 ± 1.4 mV ($P < 0.01$) lower than that in the femoral vein of the control animals. The blood cholesterol of rabbits kept on an atherogenic diet was on the average 53 mg% greater than in the control rabbits ($P < 0.05$). Morphological control examination of the investigated blood vessels revealed characteristic changes of experimental atherosclerosis in the vessel wall. The most marked morphological changes were found in the abdominal aorta and femoral artery, in agreement with observations made by other workers [10, 11].

The results indicate that atherosclerosis lowers the electrical activity of the vessel wall, and it does so to the greatest degree in the abdominal aorta and femoral artery, i.e., where the greatest changes are found in the intima in atherosclerosis [10, 11]. The smaller changes in electrical activity of the inferior vena cava in atherosclerosis correlate with the very slight morphological changes observed there in atherosclerosis [11]. Results obtained by several investigators suggest that the vessel wall should be regarded as a biological membrane through which ions of the blood electrolytes are transported [4, 9]. Furthermore, the electrical activity of the vessel wall may be generated as the result of differences in the permeability of the cells of the intima and adventitia and, consequently, of a difference in their polarity [9]. Ion transport can be considered to be disturbed by atherosclerotic changes in the blood vessel wall. As a result, the electrical activity of the vessel wall is reduced. This leads to a decrease in the intensity of transvasal electrolytic dissociation of the coagulation factors of the blood and other electrolytes. These processes are undoubtedly associated with the lowered level of metabolism in the vessel wall, which is reflected in the magnitude of its potential difference. A decrease in the potential difference between the intima and adventitia of a blood vessel have been shown to promote intravascular thrombosis [13]. Hence it follows that a decrease in the potential difference between the intima and adventitia of blood vessels in atherosclerosis may be the direct cause of intravascular thrombosis. The possible role of morphological changes in the intima, facilitating adhesion and aggregation of platelets on its surface, in thrombogenesis during atherosclerosis likewise cannot be ruled out.

LITERATURE CITED

1. V. Kh. Anestiadi, Atherosclerosis of Arteries [in Russian], Kishinev (1967).
2. N. N. Anichkov (Editor), Atherosclerosis and Coronary Insufficiency [in Russian], Moscow (1956).
3. A. A. Markosyan and A. K. Chepurov, Byull. Éksperim. Biol. i Med., No. 5, 39 (1969).
4. A. A. Markosyan and A. K. Chepurov, Fiziol. Zh. SSSR, No. 7, 816 (1969).
5. A. L. Myasnikov, Essential Hypertension and Atherosclerosis [in Russian], Moscow (1965).
6. T. Anastassiades and O. Denstedt, J. Atheroscler. Res., 7, 37 (1967).
7. S. Byers and M. Friedman, Proc. Soc. Exp. Biol. (New York), 115, 436 (1964).
8. I. Gore and F. Stare, Circulation, 25, 753 (1962).
9. D. Harshaw, H. Liskind, R. Mazlen, et al., Circulat. Res., 11, 360 (1962).
10. D. Kim and K. Lee, in: Symposium on Causal Mechanisms in Atherosclerosis and Thrombosis, New York (1963), p. 73.
11. I. Kirk, in: Biophysical Mechanisms in Vascular Hemeostasis and Intravascular Thrombosis, New York (1965), p. 244.
12. C. Preventice, G. McNicol, and A. Douglas, J. Clin. Path., 19, 154 (1966).
13. P. Sawyer and H. Deutch, Am. J. Physiol., 3, 14 (1953).
14. T. Stevenson, G. Schrodt, and L. Reed, Am. J. Med. Sci., 241, 632 (1964).
15. A. Studics, K. Reber, and H. Lorez, Path. Microbiol. (Basel), 27, 287 (1964).
16. R. Taborsky, J. Theor. Biol., 16, 147 (1967).