ACTIVATION OF THE KININ SYSTEM AS A POSSIBLE CAUSE OF HEMODYNAMIC CHANGES OCCURRING WITH THE EXTRACORPOREAL CIRCULATION

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In experiments on rabbits perfused with blood from a glass continuous-flow reservoir a sharp fall in arterial pressure and pH of the blood was observed. The plasma kininogen level also fell. These changes were absent if blood was perfused through a siliconized glass reservoir; the kininogen index under these conditions remained unchanged. It is concluded that the changes observed were due to activation of the system of hypotensive polypeptides by the glass surface of the reservoir.

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The object of this investigation was to analyze the hypotensive effect arising under extracorporeal circulation conditions in rabbits perfused with blood from a glass continuous-flow reservoir.

EXPERIMENTAL METHOD

A thermostatically controlled glass reservoir was constructed and continuously perfused with blood. Under acute experimental conditions (25 experiments) the inlet of the reservoir was connected with the carotid artery and its outlet with the external jugular vein. Electrodes were built into the reservoir for measuring the pH of the blood, and a connection for a mercury manometer was provided for recording the flow pressure. The pressure in the animal's femoral artery and the rectal temperature (by means of a thermistor) were recorded.

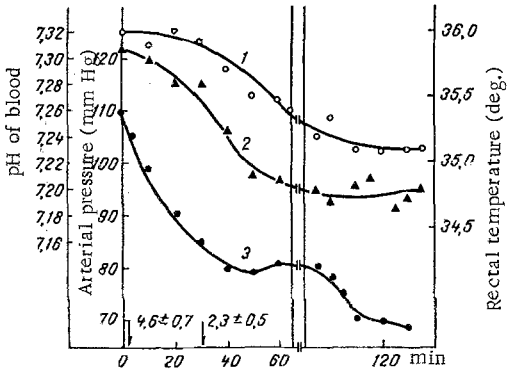

Fig. 1. Changes in arterial pressure (1), blood pH (2), rectal temperature (3), and kininogen level in experiments involving perfusion with blood from a glass continuous-flow reservoir. Numbers below represent kininogen level in μg bradykinin/ml plasma.

Experiments were carried out on male rabbits weighing 3.0-3.5 kg anesthetized with nembutal. Heparin (Richter) was used to prevent the blood from clotting. The reservoir was made from molybdenum glass, its volume was 22 ml, and a constant temperature of 37° was maintained in it.

EXPERIMENTAL RESULTS AND DISCUSSION

The first series of experiments revealed unstable working of the system: immediately after perfusion of blood through the reservoir began, the general systemic pressure gradually fell, reaching a level of 50-70 mm Hg after 30-50 min. A decrease in the pH of the blood was also observed. The rectal temperature, which usually falls steadily in a fixed animal under acute experimental conditions, in some cases reached 34-35° (Fig. 1). All these facts suggested that the changes observed could be the result of activation of the kinin system through contact of the blood with the glass surface.

Armstrong and co-workers [1] and Margolis [3, 4] showed in experiments in vitro that after contact with foreign surfaces (especially glass) a biologically active substance is

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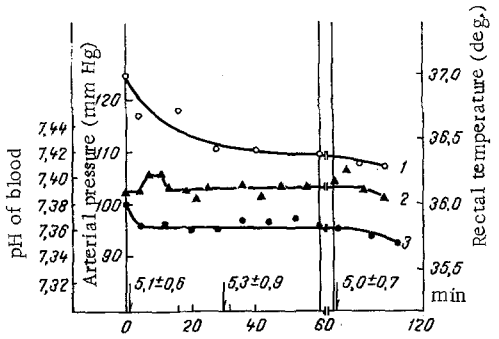

Fig. 2. Changes in arterial pressure (1), blood pH (2), rectal temperature (3), and kininogen level in experiments with perfusion of blood from siliconized glass reservoir. Numbers below denote kininogen level in μg bradykinin/ml plasma.

liberated in plasma and this was subsequently identified as bradykinin. Determination of the kininogen level by Diniz's method showed in the present experiments that 20-30 min after starting perfusion through the cuvet the plasma kininogen concentration fell by half. Hemodynamic and biochemical changes similar to these described above were also observed in control experiments in which trypsin and padutin, known to be specific liberators of active kinins, were injected into the system.

Subsequent experiments were carried out with the same glass continuous-flow reservoir, but its inner surface was siliconized (mark ZhS-5 silicone). In these experiments no significant change took place in the arterial pressure during the period of observation, the blood pH was relatively stable, and the decrease in rectal temperature was much less marked. The plasma kininogen level also remained substantially unchanged (Fig. 2).

These results indicate that the changes observed in the hemodynamic system in the experiments of series 1 were the result of activation of the kinin system by contact of the blood with the glass surface. Kinins liberated in an active form have a hypotensive action, change cell permeability, cause contraction of peripheral capillaries, and so on, and these factors evidently determine the hemodynamic changes recorded in the experiments.

This series of experiments thus confirmed, but on a different biological model, the concept of activation of kinins by glass. This fact must be borne in mind in experimental and practical work with glass surfaces, especially with extracorporeal circulation systems, because substances preventing coagulation of the blood do not exclude activation of the kinin system by glass and by other foreign surfaces.

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