THE PHYSIOLOGICAL SIGNIFICANCE OF RETRACTION OF THE BLOOD CLOT

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The process of blood coagulation consists essentially of the formation of a blood clot. This is followed by retraction of the clot, during which it shrinks sharply and expresses the serum, and finally the clot undergoes lysis as a result of the action of a proteolytic enzyme, fibrinolysin, which splits fibrin.

It is not known how the organism receives information concerning the onset of hemostasis and the subsequent course of thrombus formation, or how information leading to mobilization of the factors preventing further growth of the thrombus and to its subsequent lysis is returned.

The starting point of the search for the answers to these questions was the fact that the retraction process in the clot is accompanied by liberation of a certain quantity of serum into the blood, and the possibility has been admitted that the return of information may take place by means of this retractile serum, which may contain an active substance transmitting such information.

The present article describes the results obtained during the study of this problem.

EXPERIMENTAL METHOD

Experiments were carried out on sexually mature rabbits weighing from 2 to 3 kg. Blood for analysis was taken from the heart by puncture.

The test tube in which clotting and retraction of 5 ml of whole blood took place was incubated at 37°. After 2 h, 2 ml of the retractile serum formed was injected into rabbits, into the marginal vein of the ear.

Determination of the free heparin concentration (by Szirmai's method), the concentrations of antithrombins II and III (by the method of Witte and Direnberg) and fibrinogen, and the fibrinolytic activity (by the method of Gorshkova and Lomazova) in the plasma was carried out 10 and 60 min after the injection.

EXPERIMENTAL RESULTS

Intravenous injection of 2 ml of retractile serum into intact rabbits led to changes in the blood clotting system.

In the first 10 min an increase was observed in the concentration of free heparin and of its cofactor—antithrombin II, and also of antithrombin III. The fibrinogen concentration either fell slightly or remained unchanged. The fibrinolytic activity was practically unchanged. After 60 min the lytic properties of the blood were intensified: at this time the antithrombin activity was elevated by 100% on the average, and the fibrinolytic activity was increased (see figure, A). The results of this series of experiments showed that during retraction of the blood clot substances responsible for these changes are in fact liberated into the serum.

To test this hypothesis, the following series of experiments was performed. A blood clot formed 10-15 min after the start of clotting was taken from the test tube, carefully washed, and immersed in physiological saline. Two hours later, 2 ml of the physiological saline in which retraction of the clot had taken place was injected into rabbits. The changes developing in the blood in these circumstances were analogous to those observed after injection of the retractile serum: an increase in the heparin-antithrombin and the fibrinolytic activity took place in the first 10 min after the injections, and was still present in the blood after 60 min (see figure, B).

The hypothesis was also confirmed by the results of a series of investigations in which, instead of retractile serum, fresh serum obtained 10-15 min after the start of clotting was injected into the marginal vein of the ear.

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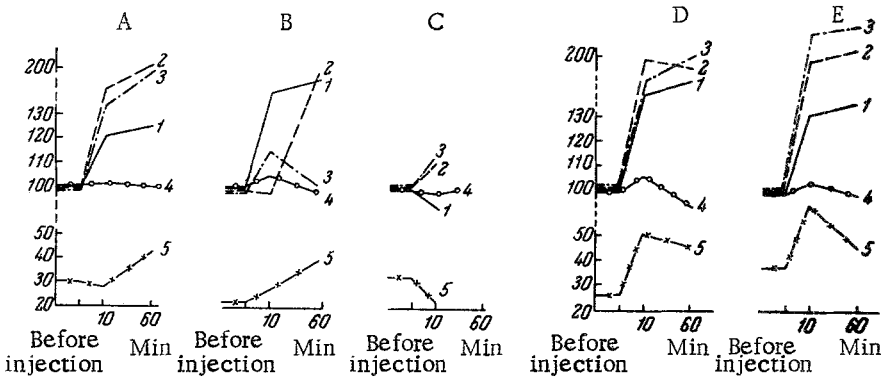

Effect of intravenous injection of retractile serum on certain indices of the clotting system of the blood. A) Effect of intravenous injection of retractile serum; B) effect of intravenous injection of physiological saline in which retraction of a blood clot had occurred; C) effect of intravenous injection of fresh serum; D) effect of retractile serum adsorbed on a 30% suspension of $BaSO_4$; E) effect of intravenous injection of dry residue obtained after lyophilization of adsorbed retractile serum and dissolved in physiological saline. 1) Concentration of free heparin (in %); 2) concentration of antithrombin II (in %); 3) concentration of antithrombin III (in %); 4) concentration of fibrinogen (in mg %); 5) fibrinolytic activity (in %).

The injection of 2 ml of fresh serum (in contrast to injection of retractile serum) caused no visible changes or actually led to a slight decrease in the heparin and fibrinolytic activity of the blood (see figure, C).

According to the findings of Quick [1], during retraction of the blood clot a serum rich in thrombin is expressed. To remove the thrombin and other thrombogenic proteins the retractile serum was treated with a 30% suspension of $BaSO_4$ for 30 min. Intravenous injection of 2 ml of the retractile serum into rabbits after adsorption with barium sulfate led to the same changes in the blood-clotting system as in the first two series of experiments. The only difference was a more marked increase in heparin-antithrombin activity (see figure, D).

It follows from the results of these experiments that the intensification of the lytic properties of the blood after injection of retractile serum is not linked with thrombin or the other thrombogenic substances adsorbed on $BaSO_4$.

In the next series of experiments an attempt was made to increase the concentration of the active substance, described as the "return information factor," without altering the volume of liquid injected. For this purpose 7 ml of retractile serum, first treated with barium sulfate, were exposed to lyophilization and the dry residue thus obtained was dissolved in 2 ml physiological saline, which was injected into the rabbits. In this series of experiments also, an increase in the lytic properties of the blood took place in the first 10 min after the injection. This increase was more marked than in the preceding experiments and the high level was maintained for 1 h (see figure, E).

The physiological significance of clot retraction has not been discovered. In 1921 Fonio [2] postulated that the main function of this process is to draw the wound edges together, thereby stopping bleeding. It was found, however, that the tractive force of the clot is too small for it to have the effect of drawing the wound edges together.

It has been suggested that on account of the retraction process the clot becomes firmer and, consequently, the thrombus when formed is more secure.

Finally, Quick [1] considers that since retractile serum contains a large amount of thrombin, the biological significance of this process lies in the further local development of thrombosis, and thereby in strengthening of the thrombus.

It may be concluded from the results of this experimental investigation that the physiological significance of retraction of the blood clot lies in the fact that during this process an active substance—the return information factor—enters the blood stream. It is neither thrombin nor any other protein component of hemocoagulation. Having entered the blood, the return information factor mobilizes the heparin-antithrombin activity and increases the

anticoagulant activity of the blood, thereby preventing growth of the thrombus and it also increases the lytic properties of the blood, leading to lysis of the newly formed thrombus.

LITERATURE CITED

1. A. J. Quick, Am. J. Med. Sci., 220, 538 (1950).
2. A. Fonio, Schweiz med. Wschr., 51, 146 (1921).