CHANGES IN THE HUMAN BLOOD CLOTTING SYSTEM CAUSED BY PROLONGED HYPOKINESIA

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An increase in the thrombogenic properties of the blood was found in the first days of prolonged hypokinesia in six subjects. This increase was connected with the stay of the healthy human subject under unusual conditions.

Changes in the clotting system of the blood followed an almost parallel course in the groups with or without physical exertion; physical exertion is evidently insufficient for preventing the changes arising in the blood clotting system during prolonged hypokinesia.

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In experiments with prolonged hypokinesia physiological responses closely resembling those under the conditions of weightlessness, one of the more important factors of space flight, can be obtained. Hypokinesia is also of interest in clinical medicine, for it is a component of the treatment of several physical diseases. However, prolonged bed rest predisposes to the development of thrombophlebitis in patients. During hypokinesia the appearance of petechiae and hemorrhages has been observed [6, 8].

Following these observations it is of practical interest to study changes in the blood clotting system arising during hypokinesia, to assess their risk and to point out methods for their prevention if these changes are pathological in character.

EXPERIMENTAL METHOD

Prolonged hypokinesia was produced by strict bed rest, to which six clinically healthy men aged 24-36 years were confined for 62 days. The subjects were divided into two groups. Group A consisted of three men who performed a series of physical exercises of static and dynamic character in a strictly horizontal position. Group B consisted of three men strictly immobilized in bed.

Blood was taken from a vein without a syringe into silicone-treated test tubes with 0.1 sodium oxalate solution in the ratio of 9:1. The plasma heparin tolerance [20], plasma recalcification time [9], thromboplastin time and activity of the prothrombin complex [18], the proaccelerin concentration [17], the thrombin time [7], the fibrinogen concentration [5], fibrinolytic activity [16], and platelet resistance [3] were determined, and the tourniquet test [11] and thromboelastography carried out, the results of the latter being interpreted by Harter's system. The recalcification time, thromboplastin time, proaccelerin concentration, and thrombin time were determined with the "Prothrombin Timer" instrument (Sweden). Blood was taken before and on the 8th, 28th, 46th, and 56th days of the investigation.

EXPERIMENTAL RESULTS AND DISCUSSION

The changes in the blood clotting system were found to be cyclic in character. On the 8th day, activity of the procoagulants was increased in all subjects, as indicated by a significant shortening of the thromboplastin time, an increase in activity of the prothrombin complex, a mean increase in proaccelerin of 15.5%, and an increase in fibrinolytic activity of 23.5%. The plasma heparin tolerance was increased by 10%, the recalcification time shortened on the average by 17%, and the platelet resistance increased by 3.7 times. In the subjects of group B the increase in activity of the procoagulants was confirmed by the results of thromboelastography. On the following days the differences between the subjects were inconsistent, regardless of their group. In two subjects (one from group A, another from group B) the increased procoagulant

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activity which was observed in the subjects of both groups on the 8th day was still present, on the thromboelastogram R was shortened on the average by 29% and K by 55%, the plasma heparin tolerance was increased by 37%, the recalcification time shortened by 17%, and the platelet resistance increased by 32.5%. The fibrinogen concentration was reduced by 33% and the fibrinolytic activity increased by 40%. In four subjects (two from group A and two from group B) the changes were different in character. On the 27th day the clotting power on the blood had fallen to a minimum, with a significant lengthening of the plasma recalcification time on the average by 36%, an increase in thromboplastin time of 15%, a decrease in prothrombin activity of 13%, a decrease in fibrinogen concentration of 22%, and an increase in fibrinolytic activity of 56%. The other indices likewise indicated diminished clotting power: on the thromboelastogram R was lengthened on the average by 32% and K by 26%, the plasma heparin tolerance was reduced by 83%, the thrombin time increased by 12.5%, and the platelet resistance reduced by 10%. With slight fluctuations, these changes persisted throughout the period of investigation, except for the fibrinogen concentration, which fell to a minimum on the 28th day, after which it showed a tendency to increase (by 11%) on the 46th day and the increase was significant (by 14%) on the 56th day. The increase in fibrinogen concentration is evidently a protective reaction of the body to the increase in fibrinolytic activity manifested by increased synthesis of fibrinogen in the liver cells.

An increase in the thrombogenic properties of the blood was found in these subjects on the 8th day. A number of workers have shown that during general excitation, for example during anxiety, fear, or anger, sympathicotonic responses are predominant, causing shortening of the clotting time of the blood [15, 19]. The increase in clotting power of the blood observed in the subjects on the 7th day may be explained by a stress reaction of the body to the constraint of the healthy subjects under unusual conditions. However, the increase in level of the blood procoagulants, with the possibility of thrombosis, is not sufficient to cause intravascular clotting of the blood. Depression of the physiological anticlotting system or disturbance of the integrity of the blood vessel wall is necessary [2, 3, 10].

The first days of confinement to bed are the most dangerous as regards thrombosis in the venous and arterial system [1, 4]. The most highly developed protective measure against thrombosis was the increase in fibrinolytic activity, which had risen by 20-23% on the 8th day. The change in fibrinolytic activity is connected with vasomotor changes observed during physical exercise or emotional and heat stress, or after injections of vasoactive substances [12-14].

The problem of increased fibrinolytic activity and the ways in which this develops has been inadequately studied. It has been shown that the endothelium of blood vessels contains plasmokinase, passing from it into the blood stream. The increased fibrinolytic activity in "stress reactions" is associated with liberation of activator from the endothelium [21]. The liberation of plasmokinase in the presence of vasoactive changes may be attributed to rupture of the endothelial layer of the capillaries. Under the conditions of hypokinesia a change in tone of the arterioles may lead to increased fibrinolytic activity of the blood.

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