BLOOD COAGULATION IN C-AVITAMINOSIS

Communication III. The Effect of Vitamins C, P, B_{12}, K, and Folic Acid on the Thromboplastic Activity of the Blood of C-Avitaminotic Guinea Pigs

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In our previous reports [1, 2], we demonstrated that one reason for the development of hemorrhagic diathesis in C-avitaminosis is disturbance of blood thromboplastin formation. We observed this disturbance to be caused by a decrease in the thrombotropin (plasma component activating prothrombokinase) and prothrombokinase concentration in the blood platelets. A decreased concentration of prothrombin was also observed.

In his study of the effect of C-avitaminosis on the blood coagulation system, McCraw [7] also observed a decrease in the prothrombin concentration in the blood. McCraw believes the reason for the decrease of prothrombin to be a secondary K-avitaminosis which develops in an organism fed a diet devoid of vitamin C. The synthesis of prothrombin, like that of thrombotropin, is carried out by the parenchymal cells of the liver under the control of vitamin K. When vitamin K was administered to white rats suffering from K-avitaminosis and to normal rats, the concentration of prothrombin and thrombotropin in the blood was restored to the normal indices in the first case and rose above the normal level in the second case [4, 5].

With these facts in mind, we tested the effect of vitamin K on the thromboplastic activity and on the concentration of thrombogenic components in the blood of C-avitaminotic guinea pigs.

The prothrombokinase content of the blood can be increased by stimulating hematopoiesis and the formation of thrombocytes in the bone marrow. Vitamin B_{12} and folic acid exert such an effect. When administered to normal white rats, vitamin B_{12} sharply increases the thromboplastic activity of the blood – to 200% of the normal activity [3].

We administered vitamin B_{12} and folic acid to C-avitaminotic guinea pigs in an attempt to increase the thromboplastic activity of the blood by increasing the prothrombokinase content in the platelets.

We also studied the effect of vitamin P on the coagulating system of the blood, as some authors [6] believe scurvy to be polyavitaminosis of C and P rather than simply a monovitaminosis of C.

EXPERIMENTAL METHODS

The experiments were performed on guinea pigs weighing an average of 250-300 g. A condition of C-avitaminosis was induced in the animals by feeding them the diet devoid of vitamin C which we described in the earlier reports [1, 2]. Before and at fixed intervals after we started the experiment, blood samples were taken from the jugular veins of the experimental and control guinea pigs, and the thromboplastic activity and the thrombogenic components of the blood determined. The determination methods and the modifications we introduced in order to determine the percentile content of coagulation factors in the blood of the guinea pigs are described in the previous reports [1, 2].

Vitamin B_{12} was administered in a dose of 7.5γ per guinea pig; folic acid was given each animal in a dose of 2 mg; vitamin K was administered in the form of the hydrosoluble derivative Synkayvite in a dose of 50γ; vitamin P, in the form of citrin, and pure ascorbic acid were administered, respectively, in doses of 2.5 and 5 mg per animal. The vitamins were all injected intramuscularly in all the experiments except in one case, of which special mention will be made.

EXPERIMENTAL RESULTS

The experiments performed on 35 guinea pigs showed that the administration of vitamin K, vitamin B_{12} and folic acid did not prevent the development of C-avitaminosis and the associated disturbances of blood coagulation in the animals. The animals fed a C-avitaminotic diet and given a surplus of the above-mentioned vitamins lost weight and died on the 18th-20th day. The data in

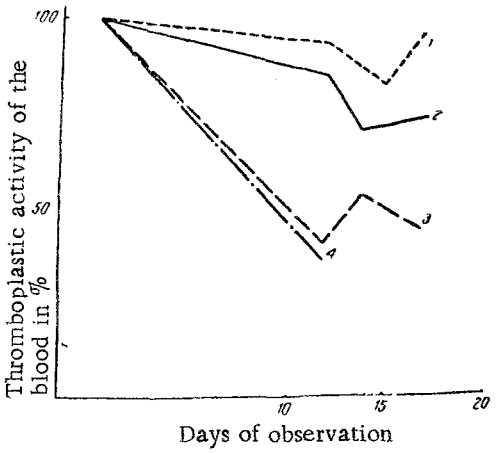

Fig. 1. Change in the thromboplastic activity of the blood of C-avitaminotic guinea pigs effected by the administration of vitamins C, K, B_{12} and folic acid. 1) Diet + 2.5 mg C; 2) diet + 7.5γ B_{12} + 2 mg folic acid; 3) diet + 50γ Synkayvite; 4) diet without additional vitamins.

the graph, however, indicate that vitamin B_{12} and folic acid do act to sustain the thromboplastic activity level of the blood. There was somewhat less change in the concentration of the thrombogenic components, prothrombin and thrombotropin, of the blood in this group than in the control. In one of the experiments, it was found that the efficiency of the vitamin C dose depends on the way in which it is administered to the organism. Although 2.5 mg, intramuscularly administered, is sufficient to effect normal development and weight gain in guinea pigs fed a C-avitaminotic diet, double this dose, i.e., 5 mg, administered per os is not sufficient to stabilize the weight. The administration per os of both vitamin C and vitamin P caused the animals to develop normally and to gain more weight than was observed with the intramuscular administration of ascorbic acid alone. The administration of vitamin P alone to the animals did not prevent the development of C-avitaminosis or the decrease in the thromboplastic activity of the blood.

It has already been demonstrated [1, 2] that the decrease in the thromboplastic activity of the blood which occurs in C-avitaminosis is due to the decrease in the concentration of thrombotropin and prothrombokinase in the blood. The results of the experiments with the administration of vitamins to animals fed a C-avitaminotic diet further demonstrate the determinant in the decrease of the blood's thromboplastic activity to be decrease in the prothrombokinase content. When hematopoiesis and the production of platelets – the source of prothrombokinase – were increased by the administration of vitamin B_{12} and folic acid, there was considerably less decrease in the thromboplastic activity of these scurvy guinea pigs than in that of the control.

The administration of vitamin K had no beneficial effect on either the thromboplastic activity of the blood or the thrombotropin level.

These data indicate that the decrease in the prothrombin and thrombotropin content of the blood of C-avitaminotic animals is evidently not due to a secondary K-avitaminosis, as McCraw proposed [7], but rather to a general decline of the synthetic processes which occurs in the absence of vitamin C.

SUMMARY

As shown by experiments conducted on guinea pigs fed a diet devoid of vitamin C, vitamin B_{12}, and folic acid administered in a daily dose of 7.5γ and 2 mg, respectively, diminished the extent of the blood thromboplastic activity reduction observed in these animals. With the administration of these vitamins, the concentration of prothrombin and thrombotropin decreased slightly less than in control experiments. Vitamin K rendered no favorable effect upon the concentration of thrombogenic components and thromboplastic activity of the blood. The efficacy of the vitamins stimulating hemopoiesis confirms the suggestion that the drop in blood thromboplastic activity is due to a reduced concentration of prothrombokinase in the platelets.

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* Original Russian pagination. See C. B. translation.