

ON CHANGES IN THE FUNCTIONAL STATE OF THE CONNECTIVE TISSUE SYSTEM ASSOCIATED WITH DECORTICATION

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Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 55, No. 2
pp. 41-45, February, 1963

Original article submitted May 31, 1962

The purpose of this work was to study the changes in the functional state of the connective tissue system associated with decortication, as well as the influence of cortisone and dibazol on the connective tissue.

Evidence of changes in the functional state of the connective tissue system due to decortication was offered in an investigation [12] showing an inertia or retardation of the processes ridding the organism of foreign substances, in animals deprived of their cerebral cortex.

The functional state of the connective tissue system was appraised from the cancerolytic and leukolytic activity of the blood serum, and phagocytic capacity of the leukocytes; also by the nature and rapidity of healing of artificially applied skin wounds. We also carried out a systematic investigation of the blood picture.

EXPERIMENTAL METHOD

The experiments were carried out on 27 male rabbits of the chinchilla family, weighing 2-2.5 kg. The animals were studied prior to decortication and the injection of cortisone, and following these actions for a period of a month.

Decortication of the animals was performed according to the method described by us earlier [1, 2].

In setting up the cancerolysis reaction, different investigators used different cells to prepare the tumor cell suspensions [3, 5, 13, 14], such as liver tumor cells, Ehrlich's mouse carcinoma cells, Jensen's rat sarcoma cells, and Brown-Pearce rabbit carcinoma cells. In these investigations, we used the method of R. E. Kavetskii [6, 11], as modified by S. P. Markin [8], employing cells from Ehrlich's ascitic carcinoma in the set-up of the cancerolysis reaction. First, the diluted ascitic fluid was mixed with the test serum, then incubated in a thermostatic cabinet at 37° for 2 h, following which we determined the percent of lysed cells.

In setting up the leukolysis reaction, we used the method described by P. A. Sakun [10]. A suspension of leukocytes, first separated from the blood by means of transient hemolysis of the erythrocytes with a 0.1% aqueous solution of eosin, was added to the test serum. The mixture of test serum and isolated leukocytes was incubated at 37° in a counting chamber, over a period of one hour, and the percent of lysed leukocytes was determined.

In the set-up for the phagocytosis reaction we used a one day old fluid culture of *Staphylococcus aureus*. A suspension of the culture, prepared according to a bacterial standard for 500 million microbial bodies, was mixed with an equal volume of citrated blood, and incubated at 37° for 30 min. The number of leukocytes showing phagocytic activity was counted in a smear prepared from this mixture.

In studying the cytogram of wound exudate according to R. E. Kavetskii and G. F. Dyadyusha [7], we judged the rate of wound healing by the increase in the number of macrophages, histocytes and profibroblasts in the smear-prints; the latter were made over a period of 4 days, starting at the moment that the wound was applied.

Depression of the functional state of the connective tissue system was brought about by cortisone; the preparation was injected twice over a period of 24 h (total dose of 40 mg/kg).

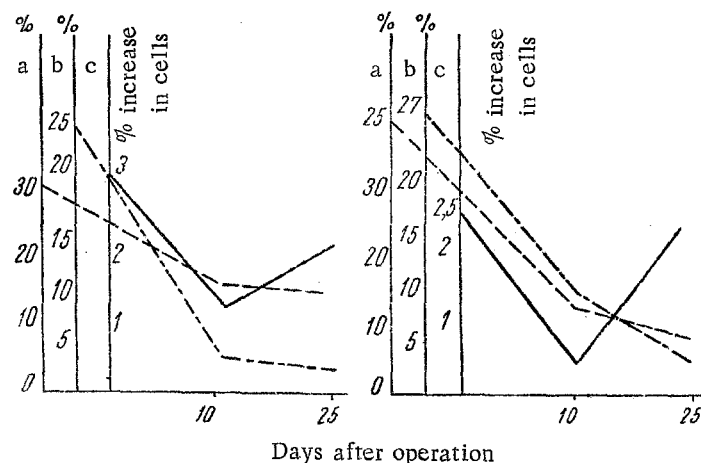


Fig. 1. Character of the changes in the phagocytic activity of the leukocytes (a), and the leukolytic (b) and cancerolytic (c) properties of the blood serum, associated with unilateral (I) and bilateral (II) decortication.

Stimulation of connective tissue functioning was performed with the aid of dibasol; the preparation was injected three times in the course of 30 h (total dose of 75 mg/kg).

EXPERIMENTAL RESULTS

The purpose of the first series of experiments was to study the functional state of the connective tissue system associated with decortication. On the 10th day after decortication, we noted depression of the connective tissue system, manifested by a lowering of the cancerolytic and leukolytic activity of the blood serum, a depression of the phagocytic capacity of the leukocytes, and a weakening and deceleration of the processes of regeneration in the skin wounds. In the animals with bilateral decortication, this depression was more profound than in the animals with unilateral decortication. It should be noted that in the rabbits with unilateral removal of the cortex we often observed asymmetry in the character of healing of the skin wounds on the right and left side; in this case the depression was usually stronger on the side contralateral to the decorticated hemisphere.

In studying the animals on the 25th day, we noted further reduction in activity of the leukolytic and phagocytic reactions, but they were now not as sharp as on the 10th day. As far as the cancerolytic activity of the serum was concerned, by the 25th day it had risen somewhat, but it did not reach the preoperative level. The character of the changes in activity of the cancerolytic, leukolytic and phagocytic reactions is presented in Fig. 1.

The changes in the blood of the rabbits as a result of decortication were not so manifest and were less regular in character. With unilateral decortication, we observed a small increase in the amount of hemoglobin, occasionally of erythrocytes, a change in the number of leukocytes, and in certain cases, an acceleration in blood coagulation. We noted a minimal leukocytosis, which was manifested more clearly on the 25th day after the operation than on the 10th. Changes in the ESR were not regular. With bilateral decortication, the blood of the rabbits showed decreases in the hemoglobin concentration, erythrocyte count and leukocyte count by the 10th day after the operation, and partial or complete normalization of these indices by the 25th day. We did not observe any manifest regularity in the changes in ESR, leukocytic formula or rate of blood coagulation.

As a specific action on the functional state of the connective tissue system, in the second series of experiments we studied the inhibitory action of cortisone on the connective tissue of normal rabbits and rabbits with bilateral removal of the cerebral cortices. We also carried out experiments on normalization of the connective tissue system functions depressed by cortisone, using dibasol.

As a result of these investigations, we observed a depressive action of cortisone on the functional state of the connective tissue system, manifested by inhibition of the reactions of cancerolysis, leukolysis, and phagocytosis. The latter was especially depressed on the 2nd day after injection of the preparation. As a rule, on the 4th day we observed a tendency toward restoration of the activity of these reactions, and on the 7th day they were completely restored. An investigation performed on the 11th day showed that this restoration was permanent and stable.

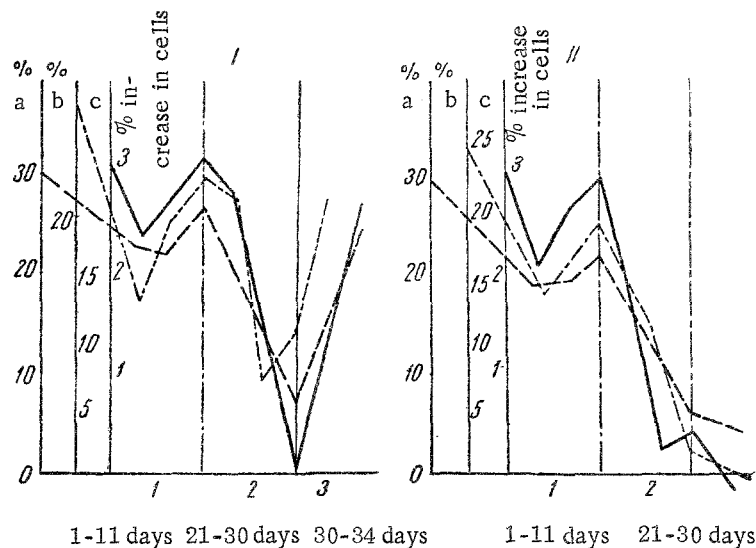


Fig. 2. Character of the changes in the phagocytic activity of the leukocytes (a), and in the leukolytic (b) and cancerolytic (c) properties of the blood serum in normal rabbits, associated with the action of cortisone (1), and in decorticated rabbits, associated with the consecutive action of cortisone (2) and dibasol (3) (I), and with the action of cortisone without the subsequent injection of dibasol (II).

Following this, we carried out bilateral decortication, which was also accompanied by a depression in the activity of the connective tissue system (on the 10th day).

On the 13th day after the operation, the decorticated rabbits were injected with cortisone, which caused a sharp depression in the activity of the indicated indices. This depression was significantly stronger than in the normal (not decorticated) rabbits, following their injection with cortisone; restoration of the connective tissue system functions studied did not occur over the course of 7 days.

Injection of dibasol on the 9th day after administration of the cortisone caused a clearly manifested stimulation of the functional state of the connective tissue system in the rabbits, as seen by a marked rise in the activity of the cancerolysis, leukolysis and phagocytosis reactions. In the decorticated rabbits not receiving dibasol, the level of these reactions remained extremely low. The character of the changes in the activity of the cancerolytic, leukolytic and phagocytic reactions, associated with the action of cortisone, decortication, and dibasol, is illustrated in Fig. 2.

We observed a decrease in the number of erythrocytes and leukocytes, and in the hemoglobin concentration, upon injection of cortisone into the normal and decorticated rabbits, and normalization of these indices following the injection of dibasol. Cortisone markedly slowed blood coagulation, which in contrast to all the other indices, was restored in the normal rabbits on the 11th day, rather than the 7th. The injection of dibasol into the decorticated rabbits succeeded in completely restoring the normal rate of blood coagulation.

The results of these experiments were treated mathematically, according to Student-Romanovskii [9], and were shown to be statistically significant.

Thus, the functional state of the connective tissue system is markedly depressed under the conditions of decortication. In tests of its activity on the connective tissue of decorticated animals, it was shown that cortisone causes a profound depression, and that the subsequent injection of dibasol leads to normalization of its function.

SUMMARY

The change of the functional state of the connective tissue system in decortication was studied by staging the carcinolysis, leukolysis and phagocytosis reactions, as well as by inquiring into the nature and rate of healing of skin wounds; the blood was analyzed in parallel.

The investigations carried out demonstrated that the functional state of the connective tissue system undergoes

considerable depression in conditions of decortication. In directed action on the connective tissue of decorticated animals it was revealed that cortisone provoked its profound depression; with the aid of subsequent dibasol administration it was possible to normalize its functions.

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