

## THE PARTICIPATION OF THE CENTRAL NERVOUS SYSTEM IN THE REGULATION OF THE BLOOD COMPOSITION

COMMUNICATION III. THE ACTION OF PAINFUL STIMULATION AND OF INJECTION OF  
ADRENALIN ON THE AMOUNT OF THE CELLULAR ELEMENTS AND HEMOGLOBIN IN THE  
BLOOD OF DOGS IN WHICH ONE OR TWO CEREBRAL HEMISPHERES HAVE BEEN REMOVED.

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(Received August 23, 1954. Submitted by V. N. Chernigovsky, Member Acad. Med. Sci. USSR)

The experimental study of the actions of painful stimulations and the injections of adrenalin on the blood picture of dogs in which one or two cerebral hemispheres have been removed has an important significance in elucidating the participation of the cerebral hemispheres in altering the blood composition under the action of pain and adrenalin. We were also interested in the problem set by I. P. Pavlov on the methods by which the cortex of the cerebral hemispheres influences the activity of the basal ganglia in connection with the regulation of the degree and duration of their stimulation and inhibition.

The experiments with painful stimulation were made on 10 dogs (5 experiments on dogs deprived of one hemisphere, 4 on dogs without two hemispheres and one experiment on a dog in which the thalamo-hypothalamic area had been damaged and the two hemispheres removed); the experiments with subcutaneous injection of adrenalin were made on 5 dogs (3 experiments on dogs deprived of one hemisphere and 2 on dogs without two hemispheres).

In dogs with one hemisphere removed the painful stimulation was produced after 23-68 days; in dogs with both removed, 18-40 days following the operation.

The adrenalin was introduced subcutaneously: in dogs without one hemisphere on the 30-36 day, and in dogs minus the two hemispheres, on the 41-53rd day after the operation.

The method of applying the painful stimulation and the injection of adrenalin are described in the preceding communications [1].

Experiments on dogs with one cerebral hemisphere. In all dogs of this series the painful stimulation produced a significant increase in the number of erythrocytes, thrombocytes and in the volume index of the blood, reaching its maximum 5-10 minutes after the cessation of the stimulus.

Five to ten minutes after applying the stimulation, the average erythrocyte number (from 3 dogs) increased by 744000 (13.5%) and that of the thrombocytes by 73000 (19%). The volume index of the erythrocytes during this time increased by 14%. Twenty to thirty minutes after the painful stimulation, the erythrocyte number, in 3 experiments out of 4, fell below the initial level. In the majority of cases the painful stimulation produced a diminution in the leucocyte number, especially pronounced after 20-30 minutes (by 24%). The number of reticulocytes was decreased in 4 experiments out of 5 (Table 1).

The longer the interval between the operation and the application of the painful stimuli, the greater was the increase in the cellular elements and hemoglobin in the peripheral blood.

The transient wave-like change in the blood picture, and especially in the number of erythrocytes after painful stimulation, was characteristic for the dogs of this series.

The alteration of the blood picture after the injection of adrenalin in dogs with one cerebral hemisphere was expressed in the following: the number of erythrocytes 15 minutes after the injection of adrenalin was diminished in one dog out of three. An insignificant increase in the number of erythrocytes and a decrease in the reticulocytes took place 30 minutes after the injection in the majority of cases. There was no special regularity in the variations in the amounts of hemoglobin, thrombocytes and leucocytes (Table 2).

TABLE 1

Blood Picture Changes After Painful Stimulations in Dogs Deprived of One Cerebral Hemisphere (the average of the findings of experiments on 5 dogs)

| Time of the experiment                | Erythrocytes<br>(in thousands) | Hemo-<br>globin(%) | Color<br>index | Volume<br>index | Reticulo-<br>cytes (%) | Thrombo-<br>cytes (in<br>thousands) | Leuco-<br>cytes |
|---------------------------------------|--------------------------------|--------------------|----------------|-----------------|------------------------|-------------------------------------|-----------------|
| Before the painful<br>stimulation     | 5530                           | 74                 | 0.67           | 0.8             | 6                      | 332                                 | 13500           |
| Following the painful<br>stimulation: |                                |                    |                |                 |                        |                                     |                 |
| After 5-10 minutes                    | 6077                           | 73                 | 0.6            | 0.91            | —                      | 440                                 | 11800           |
| After 20-30 minutes                   | 5045                           | 72                 | 0.71           | 0.76            | 5                      | —                                   | 10050           |
| After 35-45 minutes                   | 5484                           | 72                 | 0.66           | 0.81            | 3.5                    | 218                                 | 11200           |

Experiments on dogs deprived of both cerebral hemispheres. In dogs without both the cerebral hemispheres painful stimulation also produced a noticeable concentration in the peripheral blood at the expense of the increase in the number of the erythrocytes and also thrombocytes and leucocytes. After 5-15 minutes following the application of the painful stimulation, an increase in the number of erythrocytes and thrombocytes was noticed in 2 dogs out of 4; in one dog, on the contrary, there was a sharp decrease in the amounts of these elements. After 30-50 minutes following the stimulation the number of erythrocytes and leucocytes returned to normal in all dogs.

The insignificant thrombocytosis and reticulocytosis which appeared 5-15 minutes after the stimulation, were later replaced by a sharp decrease in the numbers of the thrombocytes and reticulocytes.

In all dogs the painful stimulation produced a decrease in the amount of hemoglobin (Table 3).

The changes which took place in the blood picture of these dogs after the injection of adrenalin, are analogous to those which happened after the painful stimulation, but were expressed to a more considerable extent.

Fifteen minutes after the injection of adrenalin the number of erythrocytes (the average of two dogs being taken) increased by 16%, the number of thrombocytes by 49% and of leucocytes by 13.4%.

After 30-40 minutes following the injection of adrenalin, the number of the erythrocytes returned to normal; the number of the thrombocytes and leucocytes decreased rapidly and became considerably less than the initial value (Table 4).

When painful stimulation was applied to dog No. 70 on the 37th day following the removal of the second hemisphere (previous to the extirpation of the cerebral hemispheres the thalamo-hypothalamic region of this dog was damaged on the right side), a progressive diminution of all the cellular elements of the blood and also of the hemoglobin and the volume index of the erythrocytes was produced. After 50 minutes following the painful stimulation the number of erythrocytes was decreased by 20%, that of the thrombocytes by 86% and the leucocytes by 40%; the amount of hemoglobin was lowered by 8%, the volume index by 30% and the reticulocytes were absent in the peripheral blood during 50 minutes of observation following the painful stimulation.

TABLE 2

Blood Picture Changes After the Injection of Adrenalin in Dogs Deprived of One Cerebral Hemisphere (the average findings of experiments on 3 dogs)

| Time of the experiment                   | Erythrocytes<br>(in thousands) | Hemo-<br>globin(%) | Volume<br>index | Reticulo-<br>cytes (%) | Thrombo-<br>cytes (in<br>thousands) | Leuco-<br>cytes |
|------------------------------------------|--------------------------------|--------------------|-----------------|------------------------|-------------------------------------|-----------------|
| Before the injection of<br>adrenalin     | 5387                           | 67                 | 0.83            | 12                     | 400                                 | 13200           |
| Following the injection<br>of adrenalin: |                                |                    |                 |                        |                                     |                 |
| after 15 minutes                         | 5103                           | 65                 | —               | —                      | 393                                 | 13700           |
| after 30 minutes                         | 5530                           | 64                 | 0.83            | 8                      | 335                                 | 12000           |

TABLE 3

Blood Picture Changes After Painful Stimulation in Dogs Deprived of Both Cerebral Hemispheres (the average findings of experiments on 4 dogs)

| Time of the experiment                | Erythrocytes<br>(in thousands) | Hemo-<br>globin(%) | Volume<br>index | Reticulo-<br>cytes (%) | Thrombo-<br>cytes (in<br>thousands) | Leuco-<br>cytes |
|---------------------------------------|--------------------------------|--------------------|-----------------|------------------------|-------------------------------------|-----------------|
| Before the painful<br>stimulation     | 4750                           | 59.5               | 0.37            | 6                      | 606                                 | 8950            |
| Following the painful<br>stimulation: |                                |                    |                 |                        |                                     |                 |
| after 5-10 minutes                    | 5180                           | 58.5               | 0.43            | 8                      | 696                                 | 9270            |
| after 15-25 minutes                   | 4750                           | 55                 | —               | 3                      | —                                   | 8300            |
| after 31-50 minutes                   | 4617                           | 54                 | —               | 3                      | 350                                 | 8800            |

TABLE 4

Blood Picture After the Injection of Adrenalin in Dogs Deprived of Both Cerebral Hemispheres (the average findings of experiments on 2 dogs)

| Time of the experiment                   | Erythrocytes<br>(in thousands) | Hemo-<br>globin(%) | Reticulo-<br>cytes (%) | Thrombo-<br>cytes (in<br>thousands) | Leuco-<br>cytes |
|------------------------------------------|--------------------------------|--------------------|------------------------|-------------------------------------|-----------------|
| Before the injection of<br>adrenalin     | 4305                           | 57                 | 1                      | 480                                 | 13500           |
| Following the injection<br>of adrenalin: |                                |                    |                        |                                     |                 |
| after 15 minutes                         | 4990                           | 57.5               | 1                      | 715                                 | 15310           |
| after 30-40 minutes                      | 4220                           | 56                 | 0                      | 365                                 | 11700           |

Such a distorted reaction in response to painful stimulation was shown to a much greater extent and lasted longer in dog No. 70 than in dogs in which only the thalamo-hypothalamic area had been damaged.

In all dogs with one missing hemisphere, the painful stimulation produced a decrease in the heart rate directly after the cessation of the stimulation, on an average, to 94 from 145 beats per minute; the bradycardia lasted for 15-25 minutes, after which this index became normal.

As distinct from painful stimulation, the injection of adrenalin produced, in all three dogs with one missing cerebral hemisphere, a quickening of the rhythm of the cardiac contractions from 125 to 142 per minute 15 minutes after the injection and up to 148 after 30 minutes.

In dogs with both the hemispheres missing, the painful stimulation produced a significant quickening of the heart rate (maximal after 15 minutes following the cessation of the stimulation) and of respiratory rate (maximal after 5-10 minutes).

The reaction of sham rage in dogs without one hemisphere and especially in dogs deprived of both hemispheres, disappears rapidly after stopping the painful stimulus.

While normal dogs during 30-40 minutes after the painful stimulation are in a condition of half sleep, in dogs without one hemisphere a significant shortening of the depression after the pain is produced, and in dogs without the hemispheres this condition is almost completely absent.

#### DISCUSSION OF RESULTS

If the results of the experiments conducted are compared with the findings obtained from normal dogs, it can be seen that the changes in the blood picture after painful stimulation and injection of adrenalin are considerably different. While in normal dogs the increase in the amounts of erythrocytes, thrombocytes and hemoglobin (after painful stimulation and the introduction of adrenalin) takes place comparatively slowly and lasts for 40-60 minutes and longer, in dogs in which one or two cerebral hemispheres have been removed, it has a transitory character; often after 20-30 minutes following the cessation of the stimulation, the amount of these elements falls below the initial level.

The rapid disappearance of the effect of stimulation (the change in the blood picture), produced by the painful stimulation of the injection of adrenalin, is especially noticeable in dogs without hemispheres. The latter can no longer make the fine and appropriate adjustments of the internal medium to carry out the various defensive reactions of the organism. This is indicated by the considerable diminution in the amounts of the hemoglobin, thrombocytes and, partly the erythrocytes after 20-30 minutes following the painful stimulation. The widespread idea that the removal of both hemispheres produces an increased reactivity of the vegetative centers of the subtuberal and bulbar parts of the brain, obviously required substantial correction. In any case, the changes which take place in the blood composition of dogs deprived of both hemispheres after painful stimulation do not show that the excitability of the vegetative centers of the brain and spinal cord has been increased.

It would be more correct to speak of a "chaotic" activity of the vegetative centers of the brain in relation to stimulation as well as inhibition after the removal of the cerebral hemispheres.

A sharp inhibition of the hemopoietic system, shown by the development of a persistent anemia, a lowering of the mobilizing ability of the blood system in blood losses and the lowering of the tone of the respiratory and vasomotor centers in dogs without cerebral hemispheres, point to the fact that the cerebral hemispheres carry out an important part in the normal functioning of the vegetative centers of the brain and spinal cord.

The sharp diminution of the blood indices after painful stimulation in dog No. 70, in which the removal of both hemispheres coexisted with damage to the thalamo-hypothalamic area, compared with that of dogs without hemispheres or with dogs in which only the thalamo-hypothalamus had been damaged, shows that the blood picture change observed after painful stimulation is connected with the change in the functional state of the cerebral hemispheres and of the thalamo-hypothalamic region of the brain.

#### LITERATURE CITED

- [1] N. S. Dzhevadyan, *Byull. Eksperim. Biol. i Med.* 1955, No. 5, 20-26.